UNIVERSITÀ
DEGLI STUDI
DI PADOVA

DIPARTIMENTO
DI INGEGNERIA
DELL'INFORMAZIONE

DEPARTMENT OF INFORMATION ENGINEERING

GRADUATE COURSE IN BIOENGINEERING OF REHABILITATION

Assessment of the VIKTOR method based on AFESK™ technology through analysis of electromyographic tracing, before and after treatment, on patients with neurological diseases and/or trauma.

Supervisor: Prof. Zimi Sawacha

Graduate Student: Martina Toppao

Correlators: Prof. Fabiola Spolaor
Dott. Achille Belfiore

ACADEMIC YEAR 2022 – 2023
Graduation Date 12/12/2

ABSTRACT

English Version

Nowadays, neurological diseases and trauma are an important source of temporary or permanent disability and premature mortality. Therefore, emerges the need to implement advances in the prevention of neurological diseases and trauma and to develop new methodologies for the care and rehabilitation of people who are no longer able to perform the simple actions of daily life. In this regard, neuromotor rehabilitation represents a very important rehabilitation branch for the restoration of lost function. One methodology used in motor rehabilitation for the recovery of motor deficits is electrostimulation: by sending electric shocks to body muscles, muscles that are no longer able to contract as a result of disease are stimulated.

In the present study, the effectiveness of an innovative treatment, the VIKTOR method, which aims to restore motor function in patients who, due to neurological disease or trauma, have lost motor ability in certain parts of the body, is analysed by evaluating and examining an electromyographic (EMG) trace before and after treatment. The method is based on AFESK^{TM} (Adaptive Functional Electrostimulation Kinesitherapy) technology, which uses functional electrical stimulation in combination with the performance of repeated physical exercises.

Therefore, 32 muscles corresponding to those acquired for healthy subjects were analysed and then the same were processed through Matlab codes that allowed the following indices to be extracted: Dimitrov Index (FI), Timing (on-off of the signal), Duration and Peak of the Envelope (POE).

The results show that there is an effective improvement in duration, peak of the envelope and activation and deactivation times of the muscles related to the lower limbs (BFCL, GAL, GM, RF, TA, VL).

Italian Version

Al giorno d'oggi le malattie neurologiche e i traumi rappresentano un'importante fonte di invalidità, provvisoria o permanente, e di mortalità prematura. Emerge quindi la necessità di attuare dei progressi nella prevenzione delle malattie neurologiche e dei traumi e di sviluppare nuove metodologie per la cura e la riabilitazione di persone che non sono più in grado di eseguire le semplici azioni della vita quotidiana. A tal proposito, la riabilitazione neuromotoria rappresenta una branca riabilitativa molto importante per il ripristino delle funzionalità perse. Una metodologia utilizzata in riabilitazione motoria per il recupero dei deficit motori è l'elettrostimolazione: tramite l'invio di scosse elettriche alla muscolatura corporea si stimolano i muscoli che, a seguito di patologie, non sono più in grado di contrarsi.

Nel presente studio, viene analizzata l'efficacia di un trattamento innovativo, il metodo VIKTOR, che ha lo scopo di ripristinare le funzionalità motorie in pazienti che, a causa di malattie neurologiche o traumi, hanno perso l'abilità motoria in determinate parti del corpo, valutando e analizzando un tracciato elettromiografico (EMG) prima e dopo il trattamento. Il metodo si basa sulla tecnologia AFESK^{TM} (Elettrostimolazione Funzionale Adattiva Kinesiterapica) che sfrutta la stimolazione elettrica funzionale in combinazione all'esecuzione di esercizi fisici ripetuti.

Sono stati, quindi, analizzati 32 muscoli corrispondenti a quelli acquisiti per i soggetti sani e successivamente gli stessi sono stati elaborati tramite codici Matlab che hanno permesso di estrarre i seguenti indici: Indice di Dimitrov (FI), Timing (attivazione-deattivazione), Durata e Picco dell'envelope (POE).

I risultati mostrano come ci sia un effettivo miglioramento nella durata di attivazione, nel picco dell'envelope e nei tempi di attivazione e disattivazione dei muscoli relativi agli arti inferiori (BFCL, GAL, GM, RF, TA, VL).

SUMMARY

INDEX OF FIGURES

INDEX OF TABLES

1 INTRODUCTION

Nowadays, neurological diseases and trauma are a major source of temporary or permanent disability and premature mortality [1].

There has been a significant increase in the number of people with mobility disabilities in recent years. This condition is caused by two main aspects:

- increased senescence of the population, as a percentage of 23.5% of people aged 65 and older in Italy has been calculated [2];
- increase in trauma involving whole-body injury (head injury and spinal cord injury) predominantly from traffic accidents, increased by 20% in 2021 from the previous year, with a considerable upswing in the post global pandemic period from Covid 19 [3].

The ageing of population has significant social and economic implications. It can strain healthcare and social welfare systems, as older individuals often require more healthcare services and financial support in retirement.

In fact, it increases the risk of developing neurological diseases and the rate of trauma from falls or accidental injuries involving head injuries or the breaking of upper and lower limbs, resulting in the development of various forms of motor disabilities. It was estimated that people with disabilities, in 2019 in our country, amounted to 3 million 150 thousand, where 1.5 million were over 75 years old [4]. Based on the state of the art, it is expected that people with neurological diseases or involved in different types of trauma will increase in countries where the elderly population is continuously growing, such as Europe and especially Italy [5].

Disabilities can have wide-ranging impacts, not only on the individuals who experience them but also on society as a whole in terms of economic costs, social inclusion, preventive measurements, accessibility and also employment opportunity.

So, emerges the need to implement advances in the prevention of neurological diseases and injuries and to develop new methodologies for the care and rehabilitation of people who are no longer able to perform the simple actions of daily life. In this regard, neuromotor rehabilitation represents a very important rehabilitation branch for the restoration of lost function.

Neuromotor rehabilitation aims to accelerate the progress of motor and cognitive recovery in people who have problems with balance, strength, coordination, as well as memory, attention

or language, as a result of disease or trauma. This branch of rehabilitative medicine aims at the recovery of sensory-motor and cognitive deficits, the containment of related disabilities, in order to improve the patient's quality of life and reintegration into social life. Its goals are:

- prevent or slow the loss of function;
- improve or aid in the recovery of function;
- compensate for loss of function;
- maintain current function.

One methodology used in motor rehabilitation for the recovery of motor deficits is electrostimulation: by sending electric shocks to the body's muscles, it goes to stimulate muscles that, as a result of disease, are no longer able to contract. In addition, the concept of neuroplasticity, or the brain's ability to adapt to new situations and change its neural organization, is exploited [6]. Consequently, following sensory injury, trauma and brain damage, attempts are made to restore motor functions by going on to create new synaptic connections and modifying existing ones.

1.1 PURPOSE OF THESIS

In the present study, the effectiveness of an innovative treatment, the VIKTOR method, which aims to restore motor function in patients who, due to neurological disease or trauma, who have lost motor ability in certain parts of the body, will be investigated by analysing the electromyographic (EMG) signal before and after treatment. The method is based on AFESK^{TM} (Functional Adaptive Kinesitherapy Electrostimulation) technology, which uses muscle synergies in combination with the performance of repeated physical exercises.

The thesis is organized as follows:

- In chapter two the nervous system as a whole will be illustrated;
- In chapter three will be illustrated skeletal muscle and muscle contraction;
- In chapter four electrostimulation will be illustrated;
- In chapter five the VIKTOR method will be presented;
- In chapter six the movement analysis will be presented with related in-depth analysis of electromyography;
- In chapter seven the materials and methods will be illustrated;
- The results will be reported in chapter eight;

- The discussion will be reported in chapter nine;
- The conclusion will be reported in chapter ten.

2 NERVOUS SYSTEM

The Nervous System (NS) is the complex of carefully interconnected anatomical structures including the encephalon, spinal cord and nerves, which connect these organs with the rest of the body. It is responsible for transmitting signals between different parts of the body and coordinating its voluntary and involuntary, physical and psychological actions and functions [7].

At the cellular level, the nervous system is defined by the presence of a particular type of cell, called neuron, also known as a "nerve cell".

Neurons are specialized cells of the nervous system deputed on transfer, storage and processing information. They exchange information with each other by distributing and receiving electrical signals generated by currents flowing through the cell membrane. They consist of:

- cell body (or soma), a compact roughly spherical structure deputed to process information;
- dendrites, extensions of the soma with a branched structure that collect electrical signals from other neurons and transmit them to the soma;
- axons, long protuberances that project from the soma and are responsible for transmitting the signal to the dendrites of another neuron [8].

The structure through which the transfer of the electrical impulse generated by the pre-synaptic (upstream) neuron to the post-synaptic (downstream) neuron takes place is called the synapse. Two types of synapses can be distinguished: the electrical synapse, in which there is a direct junction between two neurons; the chemical synapse, where there is no direct contact and the transmission of the electrical signal occurs by means of chemicals, called neurotransmitters, through a synaptic cleft [8].

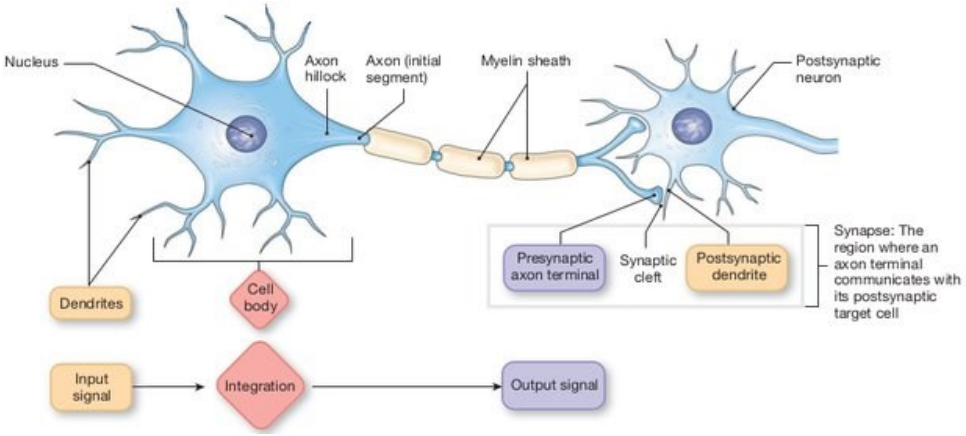


Figure 1: Neuron with its components and synapse. [9]

Connections between neurons can form neural pathways and circuits and large networks that generate an organism's "perception of the world" and allow it to determine its behaviour.

Along with neurons, the nervous system contains other specialized cells called glial cells or neuroglia (or simply glia) that do not generate and conduct nerve impulses but provide structural and metabolic support [10].

There are four types of glial cells:

- astrocytes, which act as glue and scaffolding between and for neurons;
- oligodendrocytes, which form the insulating myelin sheath around axons;
- microglia, cells responsible for immune defence;
- ependymal cells, which line the fluid-filled inner cavities.

Within the NS, it is possible to distinguish between a Central Nervous System (CNS), which includes the encephalon and spinal cord, and a Peripheral Nervous System (PNS), consisting of the nerve fibres that carry information between the CNS and other areas of the body [11].

The PNS consists of the ganglia (sets of neurons) and nerves (sets of axons) that transmit information and connect the CNS to the rest of the body [12].

The PNS is itself divided into two:

- afferent nervous system, which carries information to the CNS, informing it about the external environment and the state of internal activities that are regulated by the SNS (afferent means 'leading to');
- efferent nervous system, which carries information from the CNS to the effector organs (efferent means 'leading from').

The efferent nervous system is divided into: autonomic nervous system, which controls the smooth muscles of internal organs and glands; and somatic nervous system formed by motor neurons that innervate skeletal muscles and is responsible for voluntary movements [13].

Motor neurons induce movement and are located in the spinal cord. The axon of a motor neuron originates in the CNS and terminates on skeletal muscle. The axon terminals of motor neurons release acetylcholine (ACh), which produces excitation and contraction in the innervated muscle.

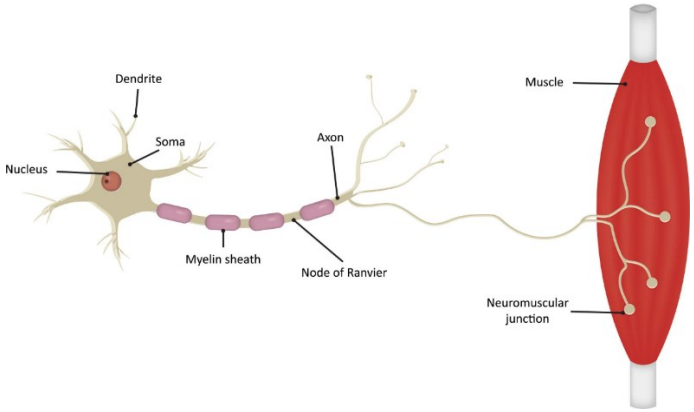


Figure 2: structure of motoneuron [14]

The CNS is a very delicate structure, which is why there are four types of structures that protect it from damage:

- bony structures, such as: the cranial box, which encloses the encephalon, and the vertebral column, which surrounds the spinal cord;
- meninges, located between the bone covering and nerve tissue and also serve as a source of nutrients;
- cephalorachidian fluid (CSF), cushioning fluid;
- blood-brain barrier (BEE), which regulates exchanges between the blood and the brain, limiting the access of blood-transporting substances from the blood.

Neurons in the CNS enable us to unconsciously regulate our internal environment by means of nerve signals, to feel emotions, to voluntarily control movement, to perceive our bodies and surroundings, and to engage in higher-order cognitive processes such as thinking and memory. Such neurons communicate with each other by means of electrical and chemical signals [11].

The CNS is also concerned with analysing information coming from the body's internal and external environment and processing responses as quickly and appropriately as possible [15].

ENCEPHALON

The encephalon consists of several structures, such as:

- brainstem;
- cerebellum;
- forebrain, which is divided into diencephalon (hypothalamus and thalamus) and brain (nuclei at the base and cerebral cortex).

The brainstem is the continuation of the spinal cord, includes the midbrain, pons, and medulla oblongata, and is responsible for vital processes such as respiration, circulation, and digestion. Attached to the postero-superior portion of the brainstem is the cerebellum, which is responsible for maintaining correct body position in space and for the unconscious coordination of motor activity (movement). It is also crucial in learning complex motor patterns. In contact with the inner part of the brain is the diencephalon, which comprises two components: the hypothalamus, which controls many functions involved in regulating the stability of the internal environment, and the thalamus, which performs initial sensory processing.

At the top of the encephalon is the brain, consisting externally of the cerebral cortex and internally of the nuclei at the base. The cerebral cortex plays a key role in nerve functions such as voluntary initiation of movement, final sensory perception, conscious thought, language, and other factors associated with the mind and intellect [11].

CEREBRAL CORTEX

The brain is divided into two halves, the left and right cerebral hemispheres, connected by the corpus callosum, a thick band formed by numerous axons.

Each hemisphere is composed of a thin outer layer of gray matter, the cerebral cortex, which covers a thick central core of white matter. Throughout the CNS, gray matter consists mainly of neuronal cell bodies and their dendrites, and most of glial cells. Bundles or tracts of myelinated nerve fibers (axons) form the white matter. The gray matter can be seen as the 'processors' of the CNS and the white matter as the 'cables' that connect the processors to each other.

Each half of the cortex is divided into four lobes, each with a specific function:

- occipital lobes, positioned posteriorly, carry out the processing of visual signals;
- temporal lobes, positioned laterally, responsible for auditory sensations;
- parietal and frontal lobes, positioned at the top of the head, separated by a deep groove, the central groove. The parietal lobes are responsible for receiving and processing sensory signals, while the frontal lobes perform three main functions: voluntary motor function, language ability and thought processing.

Sensations coming from the surface of the body are known collectively as somesthetic sensitivity (somesthetic means 'body sensation'). In the CNS this information is projected to the somatosensory cortex, located in the frontal portion of each parietal lobe. This is the initial site of cortical processing and perception of incoming somesthetic and proprioceptive impulses. Proprioception is the awareness of body position.

The somatosensory cortex of each hemisphere receives mainly sensory signals from the opposite side of the body, because many ascending pathways that carry sensory information into the spinal cord cross over to the other side before reaching the cortex. Consequently, lesion of the somatosensory cortex in the left hemisphere causes sensory deficit in the right side of the body, while loss of sensation in the left side is associated with lesions in the right cortical hemisphere.

The area in the posterior portion of the frontal lobe is the primary motor cortex. It exerts voluntary control over movements produced by skeletal muscles. Again, the motor cortex on each side of the brain controls the muscles on the opposite side of the body [11].

CEREBELLUM

The cerebellum is located below the occipital lobe of the cortex in which there are more neurons than in the rest of the encephalon, underscoring the importance of this structure. It consists of three functionally distinct parts, with different roles, primarily involved in the unconscious control of motor activity. They are:

- vestibulo-brain, important for maintaining balance;
- spino-cerebellum, which increases muscle tone and coordinates voluntary movements and is responsible for the correct timing of different muscle contractions;
- erebro-cerebellum, which is involved in the programming and initiation of voluntary activity by sending signals to cortical motor areas [11].

BRAINSTEM

The brainstem consists of the medulla oblongata, the pons, and the midbrain. All incoming or outgoing fibers that run between the periphery and the higher brain centers must pass through the brainstem. Many of these fibers make synapses in this structure, where information undergoes important processing.

The brainstem is thus a key link between the rest of the encephalon and the spinal cord. Its main functions are as follows [11]:

- it is the origin of the 12 pairs of cranial nerves that innervate the structures of the head and neck with both sensory and motor fibers;
- is home to centers of neurons that control the function of the heart and blood vessels;
- intervenes in the control of muscle reflexes involved in maintaining balance and posture.

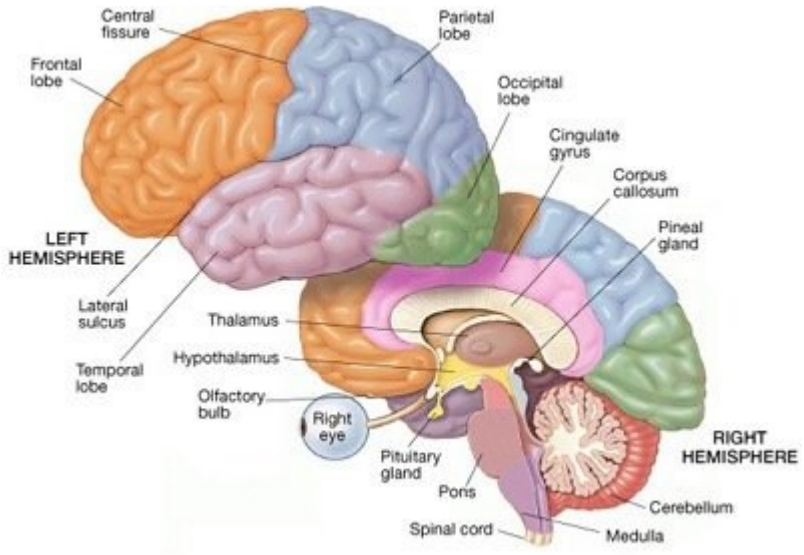


Figure 3: Encephalon and its component [16]

SPINAL CORD

The spinal cord is a long, thin cylinder of nerve tissue that extends from the brainstem. It is enclosed by the spinal column, whose function is to protect it. From the spinal cord, through the spaces formed between the bony arches of adjacent vertebrae, pairs of spinal nerves emerge.

Spinal nerves are named after the region of the spinal column from which they emerge:

- cervical spinal nerves (C1 to C8) emerge from the spinal cord in the neck and control signals directed to the back of the head, neck and shoulders, arms and hands, and diaphragm;
- thoracic spinal nerves (T1 to T12) emerge from the spinal cord in the middle and upper back and control signals directed to the muscles of the chest, some muscles of the back and many organ systems, including parts of the abdomen;
- lumbar spinal nerves (L1 to L5) emerge from the spinal cord in the lower back and control signals directed to the lower parts of the abdomen and back, buttocks, some parts of the external genitalia, and parts of the leg;
- sacral spinal nerves (S1 to S5) emerge from the spinal cord in the lower back and control signals directed to the thighs and lower parts of the legs, the feet, most of the external genitalia, and the area around the anus;
- coccygeal spinal nerves emerge from the spinal cord at the level of the coccyx and only one pair of nerves is present.

From a viewpoint of a cross-section of the spinal cord, it can be seen that the gray substance has a butterfly-shaped inner region surrounded externally by the white substance. The white substance is organized into bundles of nerve fibers with similar functions, grouped in columns that extend the length of the cord. Each of these tracts begins and ends in a particular region of the encephalon, and each conveys a specific type of information. Some are ascending tracts (from the medulla to the encephalon) that transmit signals from afferent impulses to the encephalon, while others are descending tracts (from the encephalon to the medulla) that transfer messages from the encephalon to efferent neurons [11].

NERVES

Nerves are important structures of the SNP that result from the grouping of multiple axons and have the important task of transporting nerve impulses from the CNS to the periphery, and vice versa.

Depending on the type of axons that constitute them, nerves can serve three functions: a motor function, a sensory function and a mixed function. Nerves with a motor function transmit nerve impulses from the CNS to skeletal muscles and glands; nerves with a sensory function conduct nerve impulses from peripheral anatomical districts to the CNS; finally,

nerves with a mixed function have the dual ability to act as both nerves with a motor function and nerves with a sensory function.

The main components are: axons, Schwann cells that form the myelin sheath, and lining structures with protective and nourishing functions.

There are two types of nerves: cranial nerves and spinal nerves. As seen above, cranial nerves originate in the encephalon and innervate the head and neck and there are 12 pairs in total; spinal nerves originate in the spinal cord and there are 31 pairs in total [11].

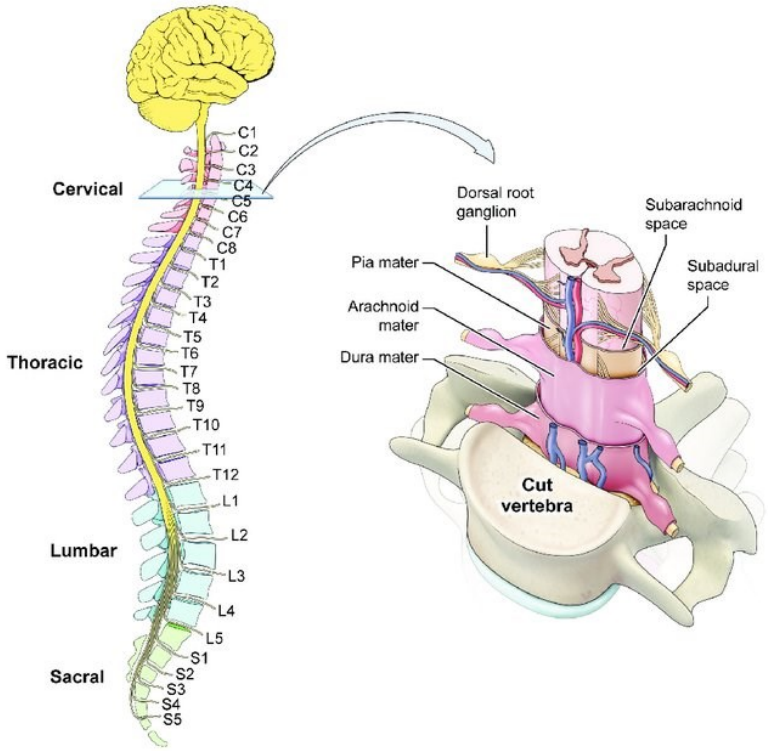


Figure 4: Anatomy of the spinal cord and vertebra [17]

As can be deduced from the above description, individual structures turn out to be very delicate with very important functions for the survival of the whole organism. It turns out to be automatic to ask the following questions: what happens if one of these structures is damaged? What are the causes that may impair their functioning? How, if at all, can the resulting pathologies be resolved? These topics are discussed in the continuation of the paper.

The medical specialty that studies disorders of the nervous system, prevention, and treatment is called neurology.

2.1 NEUROLOGICAL DISEASE

Neurological diseases are the diseases of the Nervous System, i.e., they are the afflictions affecting the encephalon, spinal cord, and/or nerves [18].

They now constitute the most prevalent disease condition in Western countries [19], characterized by a high prevalence rate and a heavy impact in terms of disability [20].

They affect one billion people worldwide, according to the World Health Organization (WHO).

A 2015 Global Burden of Disease report estimated that neurological disorders have become one of the leading causes of disability in the world, with DALY (Disability-adjusted life year), an indicator that assesses the number of active life years lost due to premature death and disability, reaching 11.6 percent and are the second leading cause of death after cardiovascular disease, reaching 16.5 percent of all deaths [21].

There are currently about 600 common, uncommon and rare neurological diseases known to affect both the CNS and the SNP. Those particularly known are: migraine, stroke, dementia, spina bifida, brain tumors, epilepsy, carpal tunnel syndrome, Alzheimer's disease, Parkinson's disease, peripheral neuropathy, and many others [12].

Major neurological diseases originate from different types of causes, among them we find:

- genetic mutations, present from birth, that originate from DNA modification. One example is Spina Bifida, a congenital malformation (present from birth) in the spine due to an error in embryonic development that can result in the leakage of meninges, spinal cord and spinal nerves, caused by the opening of the spine (bifida means 'open') [23]. Another example is Spinal Muscular Atrophy (SMA), a rare neuromuscular disease characterized by the loss of motor neurons, those neurons that carry signals from the central nervous system to the muscles, controlling their movement. It causes progressive muscle weakness and atrophy [24];
- infections due to contact with bacteria, viruses, fungi and parasites. Depending on the tissues affected, Encephalitis and Meningitis are distinguished;
- Degenerative processes, which result in the structural, morphological or chemical alteration of an organ, tissue or cell by the action of damaging factors. Among these we recognize Dementias, such as Alzheimer's disease, which involves a progressive loss of mental function, characterized by degeneration of brain tissue [25]. Another example is Parkinson's disease, a slow-moving but progressive neurodegenerative

disease that primarily involves movement control and balance and is the most common movement disorder disease [26].

- tumor-like (or neoplastic) proliferative processes due to uncontrolled growth of certain tissues or parts of the nervous system. They can be slow-growing (benign, such as meningiomas) or fast-growing (malignant, such as glioblastoma);
- immune-mediated inflammatory processes, which are exaggerated or improper responses of the immune system. An example is Multiple Sclerosis, characterized by an abnormal reaction of the immune defenses that attack certain components of the central nervous system by mistaking them for external agents [27], which leads to visual and sensory disturbances, fatigue and loss of muscle strength [28];
- trauma, which can be to the brain or spinal cord;
- epilepsy, a disease characterized by the recurrence of seizures due to an abnormal electrical discharge of a larger or smaller area of brain neurons;
- sleep disorders;
- headaches, headaches leading to conditions such as migraines;
- stroke, due to an altered blood supply to an area of the nervous system resulting in tissue death and loss of function of the affected area;
- nerve compression, due to an alteration in the normal anatomy of the elements surrounding the involved nerve, impairing its function. An example is Carpal Tunnel Syndrome, which affects the wrist nerve.

In the present study, only those neurological diseases that affect the motor ability of affected patients and are not degenerative in nature will be considered, because the treatment of a degenerative disease is only intended to slow the process and not lead to improvement.

2.2 INJURY

As mentioned earlier, one of the causes of neurological diseases that cause limitation in motor function is trauma.

Trauma is damage to the body caused by an external event, such as a collision or impact. They are very common, think of car accidents or falls, and cause various injuries that can affect the limbs, head, chest, and spine [29].

There is a wide variety of types of trauma, but the study focuses on traumatic brain and spinal cord injury.

2.2.1 TRAUMATIC BRAIN INJURY

A traumatic brain injury occurs when an external force causes trauma to the brain. It can cause physical, cognitive, social, emotional and behavioural symptoms, and the prognosis can range from complete recovery to permanent disability or death [30].

Head trauma is a leading cause of death and disability worldwide, especially in children and younger adults [31].

Different causes may include falls, traffic accidents, violent acts, and sports-related injuries. Head trauma is usually classified according to severity, anatomical features of the injury, and mechanism, that is, the type of forces that caused it. Classification by mechanism divides trauma into:

- Closed, when the brain is not exposed;
- Penetrating, when an object perforate the skull and damages the dura mater, the outermost membrane surrounding the brain.

Depending on severity, brain injuries can be classified as mild, moderate and severe. The Glasgow Coma Scale (GCS), the most commonly used system for classifying the severity of head injury, identifies a person's level of consciousness on a scale numbered 3 to 15 based on verbal, motor and stimulus response [32].

EYE OPENING	SPONTANEOUS	4
	TO SOUND	3
	TO PRESSURE	2
	NONE	1
VERBAL RESPONSE	ORIENTATED	5
	CONFUSED	4
	WORDS	3
	SOUNDS	2
	NONE	1
MOTOR RESPONSE	OBLEY COMMANDS	6
	LOCALISING	5
	NORMAL FLEXION	4
	ABNORMAL FLEXION	3
	EXTENSION	2
	NONE	1
GLASGOW COMA SCALE SCORE [33]		

MILD	MODERATE	SEVERE
13-15	9-12	3-8

Table 1: Glasgow Coma scale.

According to the Global Burden Of Disease Study there were 27.08 million new cases of traumatic brain injury per year between 1990 and 2016 [34].

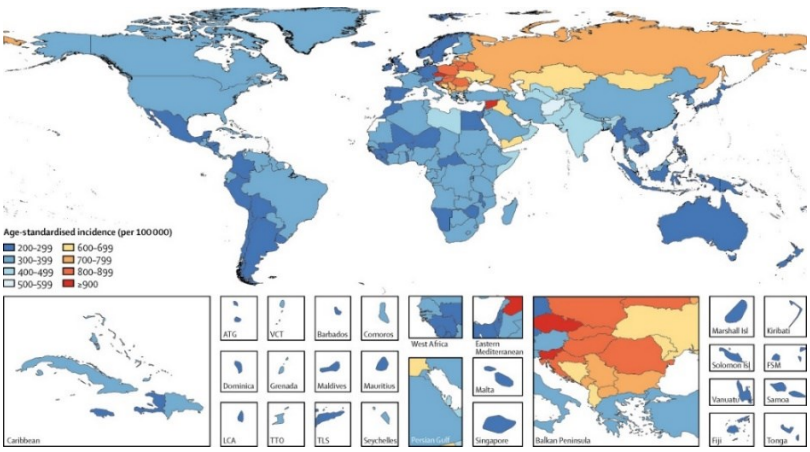


Figure 5: Age-standardized incidence of traumatic brain injury per 100,000 population by location for both sexes, 2016 [34]

The primary causes of traumatic brain injury vary by age, socioeconomic factors, and geographic region. Age-related differences among TBIs demonstrate three main age groups with the highest prevalence:

- early childhood, mainly caused by falling;
- late adolescence/early adulthood, caused by traffic accidents;
- elderly, where falls are the main cause.

Thus, it is estimated that the main cause of TBI is falls, especially in the elderly population. In addition, most studies indicate that males are much more likely to suffer a traumatic brain injury than females. The highest rate of TBI occurs in the 15-24 age group, but people younger than 5 years or older than 75 years also run a higher risk [35].

2.2.2 SPINAL CORD INJURY

Spinal cord injuries occur when soft tissue, normally protected by the vertebrae, ruptures or dislocates exerting damaging pressure on the spinal cord. Injuries can occur at any level, and the damaged segment and the severity of the nerve tissue damage will determine which body functions are compromised or lost. As a result, injury in one region causes physiological consequences to the parts of the body controlled by nerves at and below the level of the injury. For example, severe trauma to the cervical cord causes paralysis of most of the body.

Paralysis is the loss of voluntary movement of one or more muscle groups and occurs when the stimuli sent from the brain to the muscles are interrupted.

The word "paralysis" derives from the Greek παράλυσις, meaning "disabling of the nerves" from παρά (para) meaning "beside, by" and λύσις (lysis) meaning "making loose" [36].

This condition can be temporary or permanent, depending on the events that have caused it, and it can be total, when the motor function is completely compromised (plegia), or partial (paresis) [37].

Paralysis is a widespread condition. A study conducted in America in 2013 reported how 1.7% of the American population lives with paralysis. And not only in America but also throughout the world, the different forms of paralysis that exist represent a very large number. Therefore, a targeted approach is needed to both prevention and restoration of motor function, where possible, in order to return the person with paralysis to a normal living condition [38].

There are different types of paralysis based on where the problem is located:

- monoplegia if the paralysis affects a single area (for examples the face, arm and leg);
- diplegia when the paralysis is bilateral (i.e. affects two symmetrical parts of the body, such as the lower limbs);
- hemiplegia if only one side of the body is affected;
- paraplegia when both lower limbs are involved;
- tetraplegia when the paralysis extends to both the upper and lower limbs.

Many of the traumatic injuries do not result in damage to the cord but can cause fractures and/or compression of the vertebrae, which in crushing destroy few, many, or most of the axons that carry signals along the cord. Cells in and around the site of injury may also die; if there is little or no cell death there may be almost complete recovery, but if cell death is complete there may be complete paralysis.

Injury begins with primary injury, which is when the cord is stretched or displaced by bone fragments or disc material. Nerve signalling stops immediately and it may take time for it to restore itself even if there is no structural damage to the cord. In contrast, in severe injury, axons are cut or damaged beyond repair and neural cell membranes are ruptured. Blood vessels can also rupture and cause bleeding in the central tissue of the spinal cord. Within minutes, inside the spinal canal, the portion adjacent to the injury site bloat, increasing pressure on the cord and reducing blood flow to the tissue. Blood pressure can drop, sometimes dramatically, as the body loses the ability to self-regulate. All these changes can cause a condition known as spinal shock that can last from a few hours to several days or even weeks. It then initiates a cascade of biochemical and cellular events that kill neurons, remove the myelin coating from axons, and trigger an inflammatory response from the immune system. This is the beginning of the secondary injury process, which days, or sometimes even weeks, can result in an increased area of destruction, sometimes up to several segments above and below the original injury.

An injury can be classified as:

- complete, if nerve communications from the brain and spinal cord to the parts of the body below the site of injury are blocked. In this case there is a complete lack of sensory and motor function;
- incomplete, if the ability of the spinal cord to transmit messages to or from the brain is not completely lost.

Spinal cord injuries are classified by the American Spinal Injury Association (ASIA) considering motor and sensory function. Below is the scale proposed by ASIA [39].

CLASSIFICATION	DESCRIPTION [40]
UN	Complete: no motor or sensory function is preserved below the level of injury, including sacral segments S4-S5.
B	Incomplete: sensory function, but not motor function, is preserved below the neurological level and some sensation in the S4-S5 sacral segments.
C	Incomplete: motor function is preserved below the neurological level, however, more than half of the key muscles below the neurological level have a muscle grade of less than 3 (i.e., not strong enough to move against gravity).
D	Incomplete: motor function is preserved below the neurological level, and at least half of the key muscles below the neurological level have a muscle grade of 3 or higher (i.e., joints can be moved against gravity).
E	Normal: motor and sensory functions are normal.

Table 2: Classification of Spinal Cord Injury by ASIA.

It has been inferred from the literature that, based on the type of injury related to the scale proposed by ASIA, patients with an incomplete injury have a greater chance of recovering some function in the affected limbs than those with a complete injury, where therapy would have no restorative effect [41].

According to reports from a study conducted in the Veneto region in a period from January 1, 2011 to December 31, 2020, 1303 cases of TSCI were identified in this region, registering a decrease in the last year of the study due to the Covid emergency that arose in that year. That study, also reported, in agreement with other studies in the literature [42], that the cause leading to a TSCI is traffic accidents (29.9%) and occasional accidents (29.8%) and that it is more common in men than in females, with a ratio of 2.3:1. This ratio decreases with age but still remains higher for men [44].

Recovery after a spinal cord injury depends on the site (level) and extent of injury. The higher the level of the injury, the greater the physical impairment and the need for rehabilitation.

The rehabilitation of the SCI patient aims to enable the attainment of the highest possible level of function in the performance of activities of daily living and quality of life.

3 MUSCLE FISIOLOGY

Muscle constitutes the largest group of tissues in our body, forming about half of the body weight. Muscle cells are able to develop tension and contract due to their ability to coordinate contraction within the muscle. This coordinated contraction allows:

- the movement of the whole body or parts of it;
- the manipulation of external objects;
- the performance of the activities of hollow internal organs;
- the removal of substances from certain organs.

There are three different types of muscle: skeletal muscle, cardiac muscle and smooth muscle. These can be classified under two principal categories: the first to which striated (skeletal and cardiac) and non-striated (smooth) muscles belong; and the second to which voluntary (skeletal) and involuntary (cardiac and smooth) muscles belong.

Skeletal muscle forms the skeletal muscle system and is the most abundant type of muscle used for contraction; smooth muscle is used for the internal lining of hollow organs, while cardiac muscle is found only in the heart.

Specifically, a single skeletal muscle cell has an elongated, cylindrical shape that is called a muscle fibre. A skeletal muscle is the collection of numerous muscle fibres arranged parallel to each other and joined by connective tissue [11].

Each muscle fibre is made up of numerous myofibrils, specialised contractile elements that make up 80% of the volume of the entire fibre. These myofibrils are composed of two types of filaments:

- thick filaments, made up of the myofibrils;
- thin filaments, consisting of actin, tropomyosin and troponin.

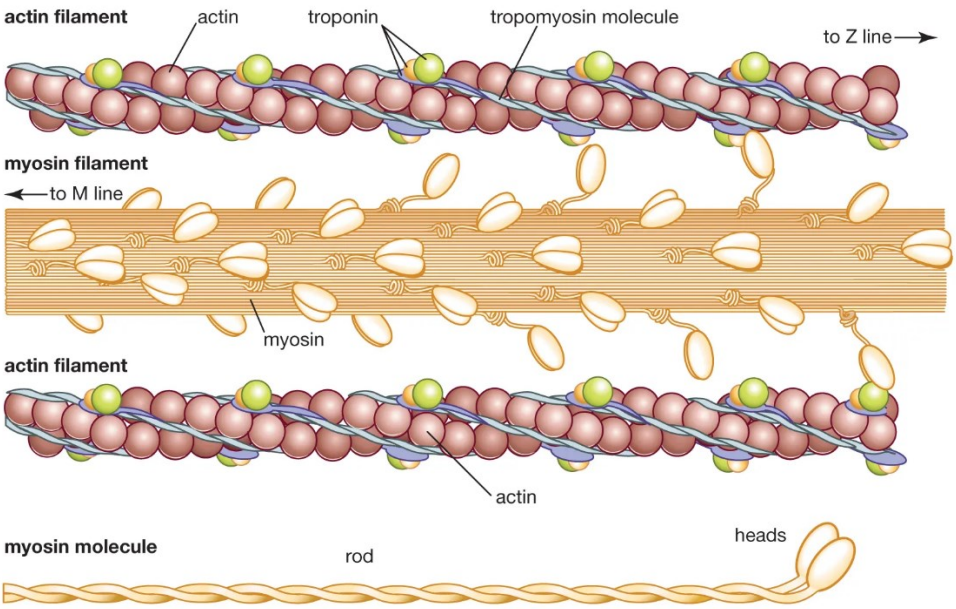


Figure 6: Actin and myosin filament and how they join together. [45]

Seen under the microscope, the myofibril shows an alternation of dark bands (A-bands) and light bands (I-bands). There is a lighter zone in the middle of the A-band, the H-band, where only the central portions of the thin filaments are found. The M-band holds the thick filaments in place in the A-band by means of proteins. The I-band, on the other hand, is formed by the remaining portions of the thin filaments that do not belong to the A-band. In the middle of each I-band, a Z-line is observed; the area between two Z-zones is called the sarcomere, the functional unit of skeletal muscle, i.e. the smallest structure capable of performing all the functions of a specific organ.

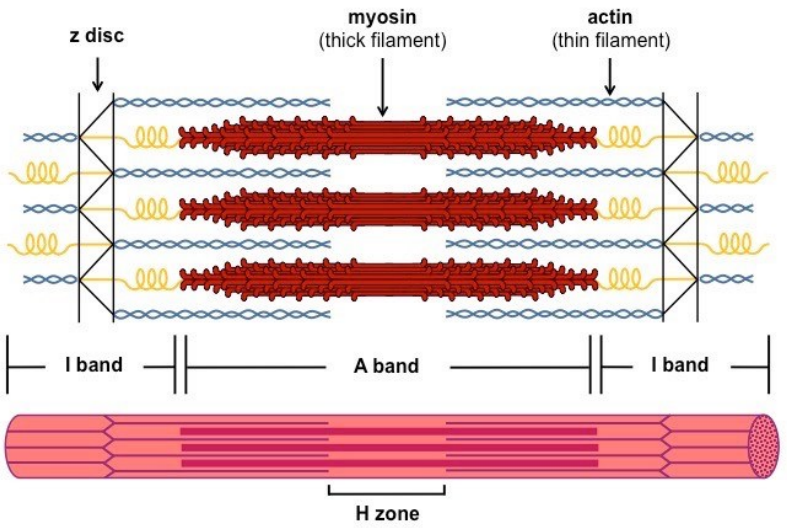


Figure 7: Sarcomere structure. [46]

Actin and myosin are the proteins specialise in muscle contraction. Specifically, myosin consists of six subunits, two of which are identical and form a terminal tail and two globular heads protruding from one end. These heads form the cross-bridges between the thin and thick filaments. Each myosin crossbridge has two important sites for contraction: a binding site for actin and a site that allows ATP hydrolysis, called ATPase.

Actin molecules, on the other hand, have a binding site in order to attach to the myosin cross-bridge. The binding between the cross bridges and the actin and myosin molecules causes the contraction of muscle fibre. When the latter is relaxed, tropomyosin and troponin cover the actin binding sites that bind the cross bridges, blocking contraction. In particular, troponin has three subunits: one binds to tropomyosin, one to troponin and one to calcium (Ca^{2+}). If troponin is not bound to Ca^{2+}, tropomyosin blocks the binding sites in the cross bridges; when, however, it binds to Ca^{2+}, troponin changes shape allowing tropomyosin to move from its blocked position. In doing so, myosin and actin bind resulting in contraction [11].

3.1 SKELETAL MUSCLE CONTRACTION

The interaction between actin and myosin through the cross bridges determines the contraction of skeletal muscle.

During muscle flexion, the thin filaments on the sides of the sarcomere slide in and over the thick filaments, pulling on the Z-lines to which they are attached in such a way as to shorten the sarcomere itself. When all the sarcomeres shorten simultaneously, contraction of the entire fibre occurs. In this situation, the cross bridges change shape, folding towards the centre of the sarcomere and causing a 'force stroke' that also pulls the thin filaments inwards. The cyclical repetition of the bonds in an asynchronous manner and the bending of the transverse bridge result in muscle contraction.

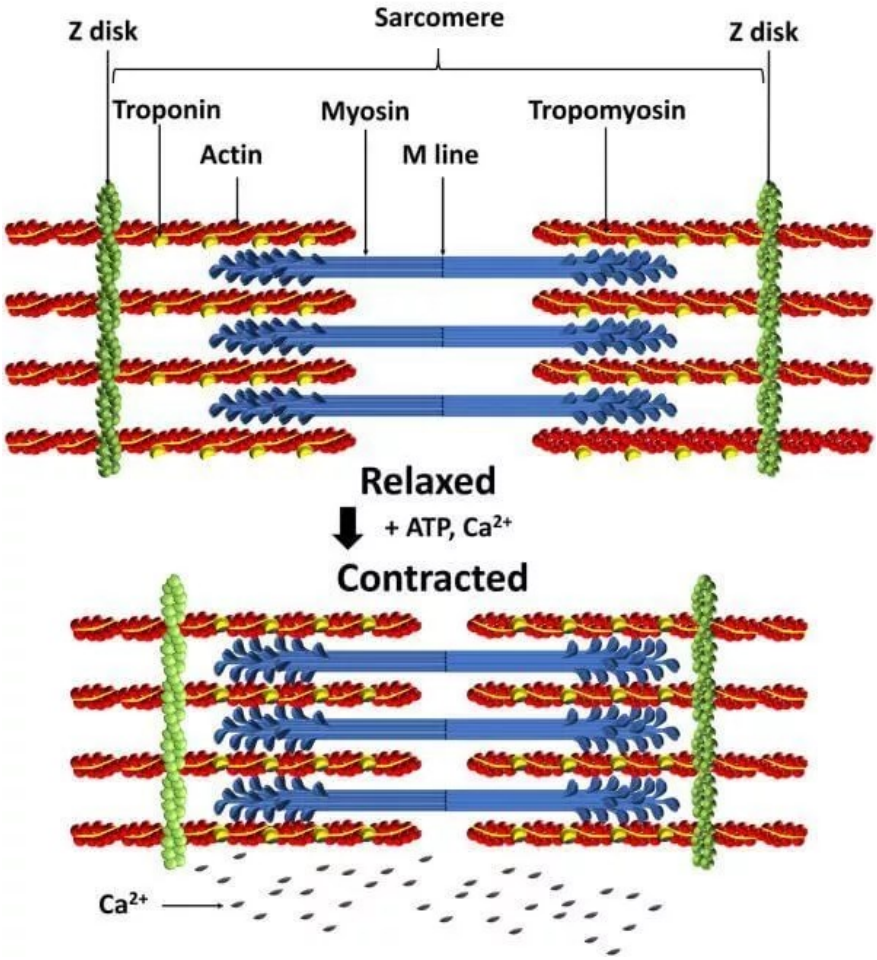


Figure 8: Visualization of sarcomere contraction. [47]

What induces muscle contraction is the electrical activity due to the release of acetylcholine (ACh). Acetylcholine is a neurotransmitter that comes from nerve cells and, via chemical synapses, is released into the muscle fibre.

When each terminal axon of the motor neuron reaches the muscle, it loses its myelin sheath and forms a specialised junction, called the neuromuscular junction. Since each axon branch innervates only one muscle cell, there is only one junction per cell. Within a neuromuscular junction, the terminal axon divides into many branches that end in an enlarged structure, called a terminal button, which contains thousands of vesicles in which ACh is located.

There are two structures that link nerve cell excitation to muscle contraction and they are: the transverse tubules (T tubules) and the sarcoplasmic reticulum. The transverse tubule crosses the membrane to the centre of the muscle fibre, so that the action potential coming from the membrane can propagate along the tubule, transmitting the surface electrical activity within the fibre. The sarcoplasmic reticulum consists of a thin network of membranes that form

closed compartments surrounding each myofibril. Segments of this reticulum surround the A-band and I-band and the end parts form sac-like regions, the terminal cisternae, separated by the T-tubules containing Ca^{2+}. The propagation of an action potential along a T tubule triggers the opening of Ca^{2+} channels that allow actin-myosin binding.

As mentioned above, myosin filaments possess two sites: an actin-binding site and an ATPase site. The second site is capable of binding adenosine triphosphate (ATP), hydrolysing it into adenine diphosphate (ADP) and inorganic phosphate (Pi). This process releases energy, creating a high-energy myosin cross-bridge that will then bind to an actin molecule.

When Pi and ADP are released after actin-myosin bonding, the ATPase site is free to bind to a subsequent ATP molecule. This new binding causes the cross-bridge to detach, which will prepare for another cycle.

Relaxation begins when the Ca^{2+} enters in the terminal cisternae. The sarcoplasmic reticulum has an energy-consuming Ca^{2+} transporter, the Ca^{2+}-ATPase pump, which actively transports Ca^{2+} from the cytoplasm to the terminal cisternae.

Muscle contraction has, therefore, its basis at a control system that is managed by the nervous system, and when talking about muscle, one cannot consider the nervous system itself. The nerve signal is transformed into a mechanical event in three stages:

- neuromuscular transmission: a nerve impulse reaching the motor plate, after releasing ACh via synapses, generates an action potential;
- propagation of the action potential throughout the muscle fibre;
- activation of contractile mechanisms.

The transmission of an impulse along a nerve fibre is an electrical phenomenon. The cell membrane of axons is polarised, which means that there are positive charges on the outside of the cell membrane and negative charges on the inside. This polarisation is due to the different concentration of Na^+ ions and K^+ ions. The Na^+-K^+ pump keeps the resting potential constant by transporting Na^+ ions outside the cell and K^+ ions inside. In this way, the amount of positive charge neither inside nor outside does not change. However, if a sufficiently high electrical stimulus is applied (above the threshold level, -50 mV), the permeability of the membrane to Na^+ increases, generating a depolarisation that causes an inversion of the internal polarity, giving rise to the action potential that propagates along the entire axon until it reaches the motor plate, where the mechanisms for muscle contraction just seen are set in motion [11].

3.2 TYPES OF MUSCLE FIBRES AND MUSCLE CONTRACTIONS

Skeletal muscle fibres are subdivided according to their speed of contraction (slow or fast) and the type of enzymatic mechanism used to produce ATP (oxidative or glycolytic). There are three different types:

- slow oxidative fibres (type I);
- fast oxidative fibres (type IIa);
- rapid glycolytic fibres (type IIx).

The fast fibres differ from the slow fibres in that the process of ATP hydrolysis is faster, consequently the rate at which energy is made available for the crossbridge cycle is also faster. Furthermore, the fibres most involved in ATP production, specifically the oxidative ones, are more resistant to muscle fatigue.

Oxidative fibres, which are slow and fast, contain a large number of mitochondria, organs involved in oxidative phosphorylation, and have a high number of myoglobin, a protein used to transport oxygen and which colours the fibres red. This is why they are also called red fibres.

Glycolytic fibres, on the other hand, have fewer mitochondria but a high content of glycolytic enzymes. They also require less myoglobin, which is why they are also called white fibres [11].

There are generally two types of contraction:

- isometric contraction, during which the external length of the muscle does not change, instead the internal length changes as there is a shortening of the Z-lines of the sarcomere;
- isotonic contraction, which in turn can be divided into: concentric, when there is an obvious external shortening of the muscle for the production of a force; eccentric, where the muscle lengthens continuously during the application of a load; isokinetic, where the movement is performed at a constant speed.

3.3 ELECTROPHYSIOLOGY OF MUSCLE CONTRACTION

The mechanics of muscle contraction occur due to the shortening of the muscle effector, i.e. the termination of an efferent nerve fibre that transmits nerve impulses to the muscle, and intensity, duration, modulation and speed depend on several factors.

The most important are:

- the muscle elongation to which the muscle is subjected before contraction and the load to which the latter is subjected;
- the number of fibres that are recruited during the contraction;
- the type of muscle fibres that make up the myofibrils;
- the amount of energy available for contraction.

Almost all of these factors are influenced by the type of motor neurons destined for the individual skeletal muscle. In fact, as seen above, each motor neuron innervates a specific number of muscle fibres, which is inversely proportional to the motor capacity of the efferent muscle: the more accurate the movements must be, the smaller the number of fibres that make up the motor unit, allowing for finer control. The speed of the impulse varies according to the structure of the nerve fibre and its diameter: in myelinated fibres, there is a higher speed due to the 'stimulus jumping' mechanism in Ranvier's nodes. In addition, the diameter of the nerve fibres reduces as one moves away from the point of entry into the trunk and therefore the periphery of each muscle will present stimuli with a lower speed than the initial portion.

The contraction of motor fibres occurs according to the 'all or nothing' law: if the action potential that is generated exceeds a certain threshold, then the whole fibre contracts, if this threshold is not reached the fibre remains inert.

Contraction force is regulated by the brain in two ways:

- by quantal recruitment or summation: smaller motor units are recruited first, followed by a progressive activation of the larger motor units. This means that during contraction, motor units are stimulated according to an increasing size and power of contraction and a decreasing resistance to fatigue;
- by rate coding: the shape and power of the contraction (voluntary and induced) depend on the recruitment and activation frequency (also known as the discharge frequency). Smaller motor units have a lower frequency range than larger units, and in this range the force generated increases as the discharge frequency increases. If a stimulus is sent to a relaxed fibre after the previous contraction, a spatial summation force occurs, so the force and speed of contraction are directly proportional to the number of fibres recruited. When contraction occurs by electrical stimulation, spatial recruitment is directly proportional to the voltage (amplitude) and duration of stimulation. It is also possible to detect temporal recruitment due to the fact that as the frequency increases,

the muscle does not have time to relax, consequently the stimuli add up over time, developing a much greater force than that developed by a single stimulus (this is referred to as tetanisation).

Electrostimulation is able to act on these recruitment mechanisms, allowing complete and continuous tetanisation of motor units [48].

3.4 MUSCLE FATIGUE

Muscle fatigue is defined as the inability to maintain the required tension in the muscles through repeated stimulation to perform a physical action. It is also seen as a motor deficit or a decline in mental function and can result from a reduction in the intensity of stimuli in the CNS and metabolic energy chain [49]. It can be measured as a reduction in muscle strength, as a change in electromyographic activity or as a depletion of contractile force.

Fatigue depends on the type of muscles recruited: some fatigue more quickly but have an equally rapid recovery time; others fatigue more slowly with a slower recovery time.

There are two types of fatigue: central fatigue and peripheral fatigue. We speak of central fatigue when there is a reduction in the number of motor units recruited and in the speed of discharge. In a normal physiological condition, there is a constant alternation of excitation and inhibition (processes regulated by the CNS) in the presence of fatigue, on the other hand, the nerve cells present a higher state of inhibition that manifests itself in a slower and weaker mechanical contraction. This is because the work of a nerve cell decreases over time and when it is under strain. In this case, the drop in voluntary maximal contraction is greater than the drop in tetanic tension. We speak of peripheral fatigue when the decrease in voluntary maximal contraction and the decrease in tetanic tension are equal. In most individuals, it is the SNP that contributes to fatigue as there may be a lack of impulse conduction in the motor axons and terminals, neuromuscular transmission at the neuromuscular junction may be reduced as a result of which conduction in the muscle fibres may also be less pronounced and the excitation-contraction mechanism may fail, resulting in a failure to contract [48].

One parameter used to extract information on fatigue is the Dimitrov index (FI), developed to assess the trend and changes in the power and frequency of muscle contractions over time.

This index is calculated by measuring:

- the signal strength, i.e. the overall amplitude of the EMG signal;
- the frequency of the signal. The frequency of oscillations can vary depending on fatigue: contractions generally start with higher frequencies and then tend to decrease with fatigue;
- the duration of the signal, i.e. the time during which the EMG signal is active. A longer duration may indicate more prolonged muscle fatigue.

The Dimitrov index makes it possible to assess and compare the course of contractions under different conditions or time points. A higher index indicates an EMG signal with high power and stable frequency, a lower index indicates muscle fatigue with reduced power and variable frequency.

4 ELECTROSTIMULATION

Depending on the diagnosis and origin of the neurological pathology and/or trauma, there are diversified treatments. Chief among them is Neurorehabilitation, which, as seen above, aims to recover sensory-motor and cognitive deficits caused by pathology and/or trauma of the central and peripheral nervous system [50].

This type of rehabilitation is carried out through a combination of manual therapies, performed by a physical therapist, and rehabilitation technologies, such as electrostimulation, through a well-designated protocol.

Electrostimulation allows working directly in the injured area, stimulating the patient's muscles and nervous system [50]. In this way, the latter can get to recover lost motor function and return to performing the simplest actions of daily life.

Electrostimulation is used [51]:

- for strength training in athletes and healthy individuals, for example, in the context of sports;
- as a rehabilitative tool in partially or totally immobilized persons;
- as a preventive technique;
- as a test to assess neuro-muscular function in vivo.

Electro stimulator impulses are transmitted through electrodes directly on the skin, simulating the action potential generally produced by the central nervous system. Hence, it is inferred, the need for proper electrode placement and good adhesion between electrodes and skin. Generally, two electrodes are used: one 'active' and one 'reference' electrode, with a lower current flow on the reference electrode. Stimulation production occurs only on the active electrode.

4.1 INDUCED CONTRACTION

The contraction-excitation mechanism can be replicated through electrostimulation, which induces action potentials in excitable cells (nerve or muscle) using electric currents. The point of application of the electric current is the motor plaque or neuromuscular junction, the point where a motor myelinated nerve fibre meets a skeletal muscle fibre. The motor plate, in addition to being a readily available anatomical point, turns out to have no myelin sheath,

which would prevent signal passage given its insulating function. A circuit is then created that will cause depolarization of the resting potential to occur, resulting in muscle contraction.

Among electric currents, two main types can be distinguished: direct current and alternating current. Not all currents, however, are capable of inducing contraction or one muscle stimulation. In particular, direct currents are not suitable for contraction because are currents with a continuous flow of charges in the opposite direction to the normal motion of electrons. They therefore turn out to be constant and unidirectional, causing an increase in temperature and ions in the tissue that can cause burns at the site where they are applied.

In contrast, alternating current is capable of periodically changing its polarities by means of an established frequency. They determine, therefore, the depolarization of the nerve fibre membrane giving rise to an action potential that, via the axon, reaches the motor plate generating an excitomotor effect capable of causing muscle contraction. Such excitomotor current can be used both in cases of motor deficit and in cases of muscle strengthening for injury prevention [48].

An important characteristic is the shape of the pulse determined by the rise time and fall time, i.e. the time necessary to go from a minimum to a maximum value and vice versa. According to this, excitomotor currents can have different forms [52]:

- rectangular pulses, where the intensity instantaneously reaches the maximum value, holds it for a certain period of time and then instantly returns to 0;

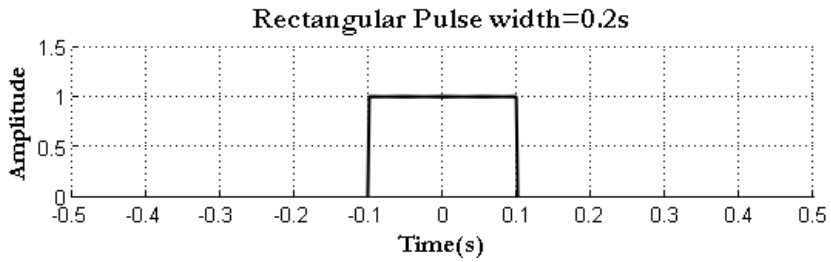


Figure 9:Rectangular pulse. [97]

- triangular pulses, where the maximum value is reached with a linear rise and then quickly returns to zero; in this type of pulse, the rise time is equal to the duration of the pulse;

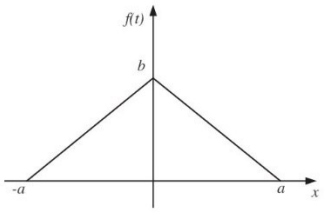


Figure 10: Triangular pulse. [98]

- exponential pulses, in which the intensity reaches maximum values gradually following an exponential pattern and then returns instantaneously to zero, the rise time is less than the pulse duration.

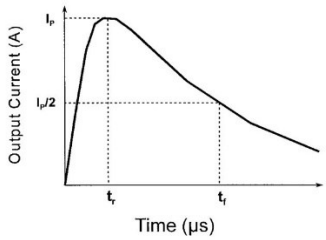


Figure 11: Exponential pulse. [99]

Then there are other types of waveforms that cannot be traced to geometric shapes, namely, faradic and sinusoidal currents. Specifically, neofaradic, sinusoidal and rectangular currents are used in stimulation of innervated muscle while rectangular, triangular and exponential currents are used to stimulate denervated muscle.

4.2 TYPES OF ELECTROSTIMULATIONS

There are two main forms of electrostimulation:

- transcutaneous electrical nerve stimulation (TENS), which aims to reduce acute or chronic pain;
- neuromuscular electrical stimulation (NMES), which aims to increase muscle contraction.

The type we will focus on is NMES.

NMES is when, to induce muscle contraction, motor neurons are stimulated either directly through mixed peripheral nerves or indirectly through reflexes. It is used to:

- strengthen muscles through resistance exercises;
- maintain or increase range of motion;
- re-educate voluntary motor function;

- inhibit spasticity and muscle spasms.

The use of electrical stimulation to activate muscle contraction or to help patients in motor activities, such as walking, constitutes Functional Electrical Stimulation (FES).

FES is used primarily in patients in whom the muscle has lost its motor control as a result of neurological disease or trauma, with the goal of providing muscle contraction leading to restoration of lost function.

For effective contraction by FES to occur, the muscle must be innervated; that is, even if the muscle has lost its central innervation, peripheral innervation must remain present.

In this case, stimulation is not limited to the execution of a single gesture that you want the patient to recover but reproduces an entire complex movement by going on to stimulate all the muscle groups that the SNS activates to perform that movement. Thus, an attempt is made to bombard the SNS with afferent information, which must then generate an efferent response.

FES is performed in the following way:

- the electrode placed on the skin creates an electric field at the point of application;
- the field produces a membrane depolarization of the surrounding neurons;
- when the depolarization reaches a certain threshold, an action potential is formed;
- this potential propagates in two directions: near nerve endings and near synaptic buttons giving rise to contraction.

Most FES applications target nerve innervation as opposed to muscle, as muscle has a larger action potential requiring a higher stimulation threshold, unlike the action potential of neurons.

Physiologically, there is first a recruitment of the smaller motor units, continuing with the larger ones. In artificial stimulation, on the other hand, lower currents activate axons with larger diameters, this is because a greater change in membrane potential is achieved.

Muscle contraction is controlled by manipulating the parameters of the current: frequency, amplitude and pulse duration. If the frequency is very high, the stimuli can add up both spatially and temporally, a situation that can be exploited to increase the force of a contraction, thus increasing the number of motor units recruited and increasing the amplitude of the pulsations, creating a larger electric field. It increases, however, the risk of muscle fatigue that would compromise the restoration of motor function. Low frequencies are therefore preferable to allow temporal summation but without having fatigue [53].

There are different waveforms for FES or for electrostimulation in general, but the waveform that is preferred is the compensated biphasic square wave, providing greater efficacy because the action potential of the muscle is triggered in a shorter time and there is greater optimization of the pulse due to the larger stimulation area. It is also safer as it provides stimulation with minimal electrical parameters. The fact that it is compensated avoids the effects of electrical polarization and therefore skin redness and burning, eliminating issues related to the thermal effect that, in patients with prostheses, can lead to internal overheating resulting in necrosis [54]. Specifically, this is the waveform used in the VIK16 machine presented in this study.

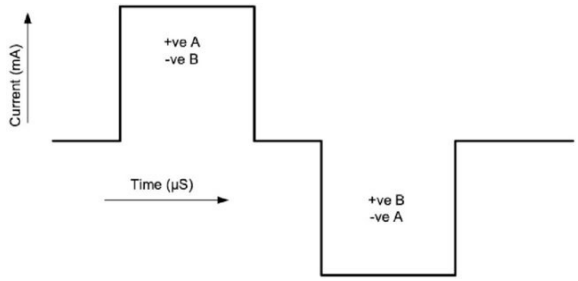


Figure 12: Schematic representation of a symmetric biphasic square wave current.[100]

In conclusion, several studies found in the literature have analysed the effectiveness of FES in different application areas.

There is evidence that the association between FES, ideation of a motor pattern and execution of the gesture leads to greater results in terms of neuroplasticity [55][56].

Other studies highlight its usefulness on wrist extensor deficits, drooping foot, reduction of spasticity and increased joint ROM (Range Of Motion) [57][58].

It has also been applied on healthy subjects, showing a correlation between electrical stimulation of the lower limbs and increased activity in certain cortical areas and how this is directly proportional to the intensity of stimulation [59][60].

On stroke subjects, intensive performance of FES led to a significant increase in hand function and an increase in cortical activity ipsilateral to the paretic hand [61].

Finally, it has been shown that there is a correlation between the duration of the rehabilitation session with electrostimulation and maintenance of cortical effects over time [62].

For all these reasons, functional electrical stimulation is the basis of the AFESK^{TM} technology on which the VIKTOR method, examined in this study, is based. In the following, the individual components of the technology and how it works are analysed in detail.

5 VIKTOR METHOD

The introduction of the VIKTOR method, devised by Dr. Terekhov Viktor, has made it possible to revolutionize the concept, limitations, effects, and use of electrostimulation [63].

As seen above, it is based on the AFESK^{TM} technology born from the meeting of functional electrical stimulation (FES), which can electrically stimulate a maximum of 16 muscle groups (synergies) to reproduce complex physiological movement, and kinesiotherapy. This means that the stimulation given by an AFESK machine allows a movement to be reproduced in its exactness through cyclic repetition. It acts on both motor and sensory components such that the nervous system is able to reactivate lost functional abilities in patients suffering from trauma or neuromuscular dysfunction, restoring or improving the organization of nerve circuits affecting the damaged body part. The technology is based on both scientific evidence [64] from years of research in the field of rehabilitation, to which are added the in-depth scientific principles developed by Dr. Terekhov, and on clinical practice. Thus, it can be said that AFESK^{TM} technology lies in the middle ground between evidence based and clinical practice.

The term AFESK stands for Functional Adaptive Kinesitherapies Functional Electrical Stimulation:

- Adaptive: modulability of the stimulus;
- Functional Electrical Stimulation: electrical stimulation delivered concurrently with functional movement;
- Kinesitherapy: high-intensity movement-based physiotherapy.

Specifically, this technology is based on several principles, such as: FES, kinesitherapy, fitness, repetition, activity-based therapy and bilateral training.

Kinesitherapy, the second pillar of the technology, allows the patient to be an active part of the treatment by actively performing each exercise. The latter must reproduce the gesture by trying to activate the muscles and cortical areas deputed to the conception and execution of the movement. If the patient is unable to actively perform an exercise (e.g., in the case of paralysis), he or she is asked to imagine the movement, contextually trying to perform it. Motor imagining, in fact, has been shown to be useful in activating certain cortical areas and increasing the plastic response centrally [65][66][67][68].

Therefore, the active part plays a fundamental role in AFESK^{TM} technology and is what distinguishes it from the other types of electrostimulations in use to date, where the patient plays a passive role [50].

Several studies demonstrate the importance of kinesiotherapy and treatment with an active approach even in individuals with severe movement impairment, with the goal of both promoting neurological recovery and improved gait in individuals with incomplete spinal cord injury [69], avoiding reduction of muscle mass by allowing the preservation and creation of as many muscle-level receptors as possible that can communicate with the SN [70].

Thus, the goal of kinesiotherapy in AFESK^{TM} technology is to focus both on the use of preserved muscles to achieve compensatory functions and on sub-injury muscle activation in order to re-train the SNS to recover a specific motor task.

The third concept underlying the method is Fitness, which allows a higher volume of work to be proposed than traditional rehabilitation (Intensive Functional Recovery). Patients, particularly neurological patients, have a reduced level of fitness (properly 'being fit, fitness') compared to the healthy population that could result in permanent disability and help from others. The high execution of repetitions, guaranteed by the AFESK^{TM} technology, allows to increase the fitness status of the treated people, causing an improvement of aerobic type and at the level of the cardiovascular system, for example, positively influencing the walking performance in people with disabilities [71][72].

From what has just been defined, another fundamental concept developed within the VIKTOR method is evident: repetition. Several studies have shown that the high number of repetitions performed for each exercise is able to induce motor learning [73] and allows faster recovery of motor patterns, such as walking, and seem to induce greater neuroplasticity, observed through fMRI [74].

Also related to neuroplasticity turns out to be the concept of Activity Base Therapy (ABT). Behrman and Harkema defined ABT as "*interventions that provide activation of the neuromuscular system below the level of injury with the goal of retraining the nervous system to recover a specific motor task*" [75][76]. Choosing from the 50 exercise programs contained within the VIK16, a workstation through which AFESK^{TM} technology is applied, allow for the selection of complex functional or sporting movements and gestures that can be selected as the outcome of the rehabilitation pathway (e.g., walking, sit to stand, reaching). Thus, the use of predetermined goals and continuous feedback provided by the technology, allow a higher intensity of work through a high number of repetitions performed by the patient in the

single session in a specific time interval. In this regard, disparate studies show that in order to improve desired functional outcomes, it is necessary to reach a certain threshold of intensity [77]. The ability to reproduce different functional gestures, from walking to reach and grasp, allows the patient to repeat specific tasks and skills having as an effect increased neuroplasticity and learning of lost complex functional gestures [78][79][80].

Finally, each program contained within VIK16 involves stimulation of both hemi-laterals of the body, promoting bilateral work. Even if the pathology has affected only one side of the body, or a portion of it, the AFESK^{TM} technology is designed to stimulate the unaffected side as well, so as to ensure a greater increase in strength in both hemi-laterals [81], a gain in long-term motor skills, and thus an improvement in neuroplasticity [82].

The aim of AFESK^{TM} technology is to promote reorganization and regeneration of the SNS in all those situations where its impairment causes movement disorders.

5.1 NEUROPLASTICITY

The pillars on which AFESK^{TM} technology is based refer to a common goal: to stimulate and promote neuroplasticity. Neuroplasticity is understood as the ability of the SNS to change its structure over time in response to interaction with external or internal stimuli.

This characteristic is manifested by changing the number and efficiency of neuronal connections at chemical synapses. It is therefore possible to manipulate the strength of these connections by varying the intensity of use of the synapse, increasing it if it is highly stimulated to create new connections (sprouting), or gradually decreasing it until it is eliminated altogether by inactivity (pruning). In addition, even after birth, neurons can create new dendritic connections with other neurons through electrical and neurochemical stimuli, consequently giving rise to new synapses. These changes between neuronal connections result in a change in the functions they regulate. Brain plasticity is present throughout the lifespan allowing for constant learning.

In both people with neurological diseases and those with orthopaedic or traumatic conditions, the SNS is affected and adapts to these abnormal conditions. It is necessary, therefore, to consider not only the muscle and joint but the neuromusculoskeletal system in its entirety, directing it toward as complete a recovery as possible in both the conception and execution of a movement [83].

Following damage, the ability of the SNS to repair and renew itself is very limited. In particular, axons within the SNP exhibit a very high degree of regeneration if the myelin sheath is partially preserved, going on to recreate synaptic connections lost, for example, in muscles.

In contrast, regeneration at the level of the CNS in adulthood is nil because repair mechanisms are triggered that hinder the reconstruction of injured circuits.

However, patients with brain or spinal cord damage can partially recover cognitive, sensory, and motor functions, as they are hypothesized to be dependent on the reorganization of synaptic connections still present and functions in undamaged brain areas.

The task of AFESK^{TM} technology is to deliver a large amount of afferent information to the CNS so as to promote adaptation and response to stimuli, with the ultimate goal of reorganizing and regenerating (or replacing) neuronal circuits damaged as a result of trauma, injury, or disease. Electrical stimulation associated with physiological movement causes the CNS to recognize movements and stimuli given to it as its own, attempting to reproduce them, promoting the appearance of new connections or reorganizing existing ones. Consequently, it improves communication between the periphery and the centre, thus enabling better motor skill and control [84].

5.2 WORKSTATION VIK16

As already anticipated, the VIKTOR method is applied by means of a 16-channel workstation called VIK16 [63], which is unique in that it is the first to feature such a large number of electrostimulation channels, to each of which a specific group of muscles is connected to realize a specific motor function.

Figure 13: Workstation VIK16. [63]

The basic location of electrodes on the major muscle groups and their respective channels is as follows:

CHANNEL	ANATOMICAL DISTRICT	MUSCLE GROUP	MOTOR FUNCTION
1	Right lower limb	Biceps femoris	Knee flexion
2	Right lower limb	Quadriceps femoris	Knee extension
3	Left lower limb	Biceps femoris	Knee flexion
4	Left lower limb	Quadriceps femoris	Knee extension
5	Right lower limb	Gluteus maximus	Hip extension
6	Back	Column erector	Spinal extension
7	Left lower limb	Gluteus maximus	Hip extension
8	Abdomen	Rectus abdominis	Flexion of the spine
9	Right arm	Biceps brachii	Elbow flexion
10	Right arm	Triceps brachii	Elbow extension
11	Left arm	Biceps brachii	Elbow flexion
12	Left arm	Triceps brachii	Elbow extension
13	Right shoulder	Anterior deltoid	Shoulder flexion
14	Right shoulder	Posterior deltoid	Shoulder extension
15	Left shoulder	Anterior deltoid	Shoulder flexion
16	Left shoulder	Posterior deltoid	Shoulder extension

Table 3: Location of electrodes and their respective channels.

It is now seen how the basic placement of electrodes on the muscle and its channel is done.

Front view

2 Right lower limb. Rectus femoris, Vasto medialis, Vasto lateralis.

4 Left lower limb. Rectus femoris, Vasto medialis, Vasto lateralis.

8 Abdomen. Abdominal rectus.

9 Right arm. Biceps brachii (long and short head).

11 Arm. Biceps brachii (long and short head).

13 Right shoulder. Anterior deltoid.

15 Left shoulder. Anterior deltoid.

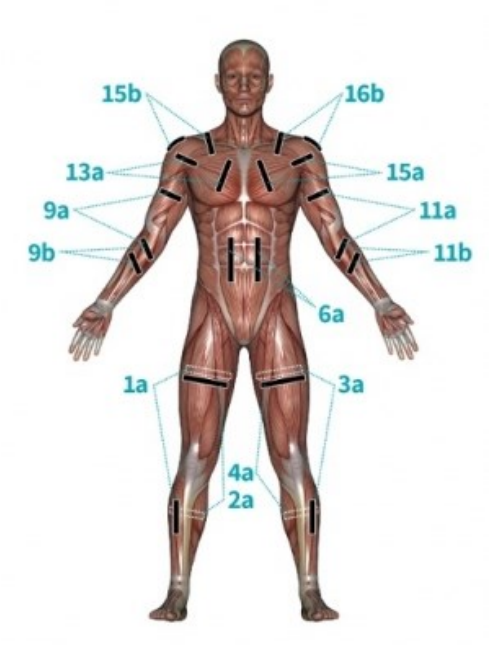


Figure 14: Front view of electrode placement. [63]

Rear view

1 Right lower limb. Biceps femoris, Semimembranosus, Semitendinosus.

3 Left lower limb. Biceps femoris, Semimembranosus, Semitendinosus.

5 Right gluteus. Great gluteus, Mid gluteus.

6 Thoracolumbar area, paravertebral position. Great Dorsal, Erector of the spine, Longus thoracis, Ileo-costalis of the loins, Multifidus.

7 Left gluteus. Great gluteus, Mid gluteus.

10 Right arm. Triceps brachii, (lateral head, long, medial).

12 Left arm. Triceps brachii, (lateral head, long, medial).

14 Right shoulder. Posterior deltoid.

16 Left shoulder. Posterior deltoid.

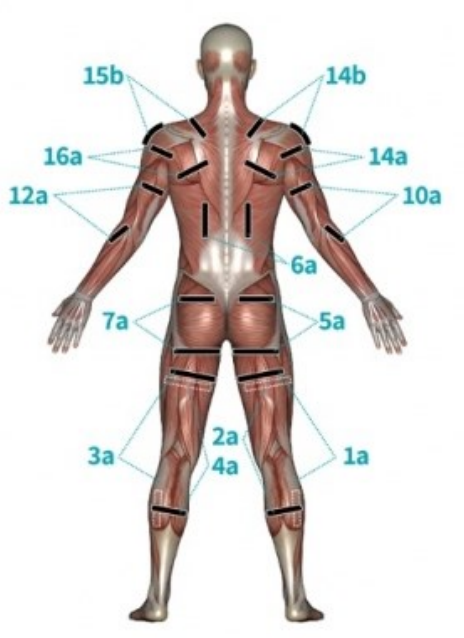


Figure 15: Posterior view of electrode placement. [63]

For adequate electrical stimulation to occur, the current parameters must be set so there is an accentuated contraction for each of the active channels in the selected program, i.e., maximum muscle contraction must be caused, preferring an increase in current from session to session as the neuromuscular apparatus gradually adapts to the electrical stimuli generated by VIK16. The workstation allows the parameters of each individual session to be stored, facilitating their use in subsequent sessions.

Depending on the patient's pathology, characteristics and condition, the VIK16 allows the creation of customized work sessions by sequentially implementing different motor programs. There is a library of 50 predefined programs, motor exercises that the patient should try to perform to his or her maximum capacity. The programs were created by evaluating the polymiography and biomechanics of movement of healthy people, considering the synergistic, reciprocal and antagonistic relationships of the moments of activation of the body's main muscle groups [85].

The VIK16 workstation makes it possible to set multiple parameters related to electrical stimulation, specifically: a stabilized current in each of the 16 channels of maximum 150 mA, a pulse duration from 100 to 1000 μs, a pulse frequency from 50 to 200 Hz, a movement cycle duration from 200 ms to 10 s, customized parameters for each muscle synergy for all exercises for both impedance and current level, and also allows customization of the number of movements and time for each exercise.

During the execution of each program, the VIK16 workstation makes available the activation of an acoustic signal to be associated with the leader channel, i.e., the channel connected to that muscle synergy that initiates the movement, in order to synchronize the movement performed by the patient with the delivery of the stimulus to the muscle. This, together with the feedback provided by the machine, allows motor function to be implemented in the cortical centers responsible for controlling movement.

The following are the 50 programs proposed by the VIKTOR method and found within the VIK16 workstation.

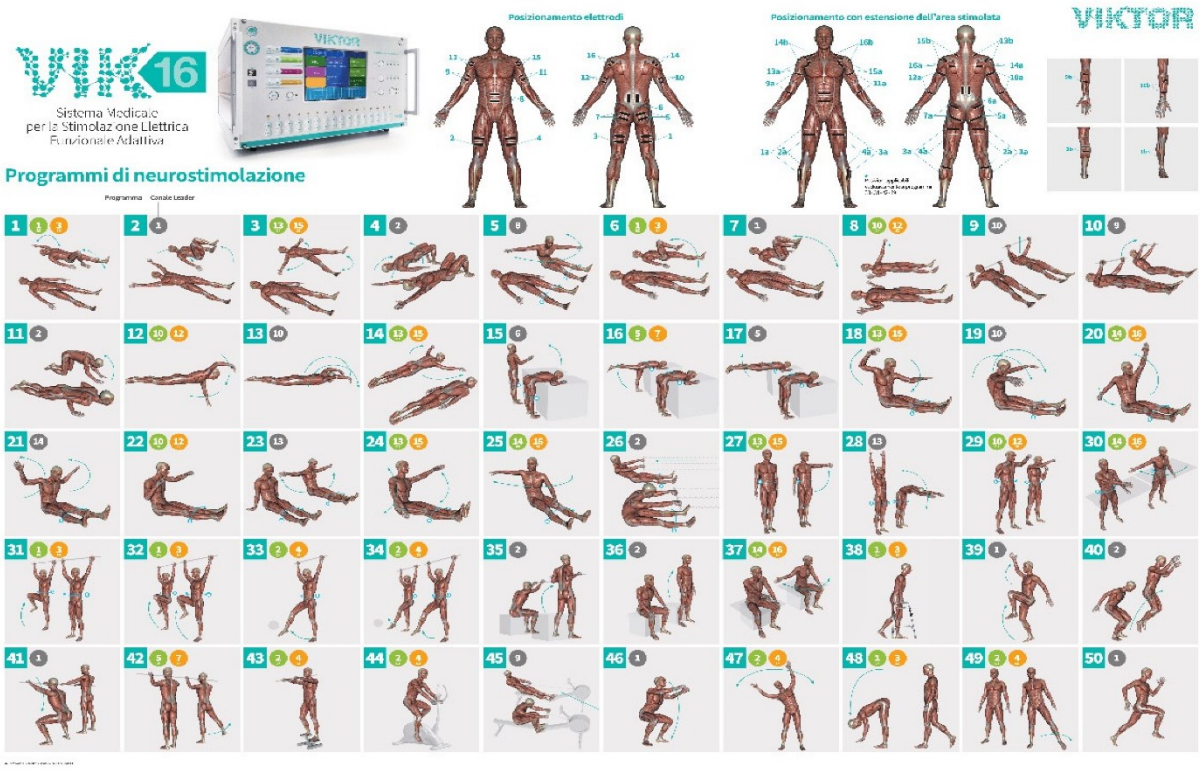


Figure 16: 50 programs proposed by the VIKTOR method. [63]

AFESK™ technology is used in the following areas:

- Neurological: spinal cord injuries [69], stroke outcomes [86], peripheral injuries [87], neurological diseases [88][89];
- Musculoskeletal: post-surgery [90], low back pain [91], musculoskeletal pain, prevention;
- Geriatric: issues related to old age, maintaining good fitness, movement deficits [92];
- Sports: performance enhancement [80], reathleticization, recovery and improvement of specific sports gesture, prevention.

6 HUMAN MOVEMENT ANALYSIS

Movement analysis provides a range of advanced technologies for the assessment of the biomechanical framework of motor gesture through the detection, processing and comparison of kinematic, dynamic and electromyographic parameters. It is used both to study functional limitations in people with diseases and in the sports field for the prevention and improvement of sports performance.

Specifically, it deals with the study:

- of kinematics, analysing motion in space, i.e., the movement of points, parts or the inside of the body and joint movements;
- of kinetics, measuring the forces exchanged with the ground and/or objects, the forces acting on tissues, pressures and muscle activations that generate movement;
- of clinical and rehabilitation, assessing motor impairment with subsequent planning of the most optimal therapy;
- of sports, analysing the sporting gesture and planning training suitable for prevention, improvement or rehabilitation.

Movement analysis is carried out through the use of various instrumentation to examine the movement of each joint and muscle synergies. These include:

- a stereophotogrammetric system, consisting of at least two cameras capable of detecting and reconstructing the position of sensors (markers) placed on the patient's skin, useful for detecting kinematic data [93];
- force platforms, which make it possible to measure the force that the subject's foot exchanges with the ground, detecting dynamic data
- pressure sensors, which describe the trajectory of the centre of pressure and the distribution of plantar pressure;
- IMU inertial sensors, which allow information on acceleration forces to be obtained;
- electromyography, which makes it possible to measure the electrical potentials that develop on the muscle during muscle contraction; useful for detecting disease and assessing motor improvement following rehabilitation [96].

6.1 ELECTROMIOGRAPHY

Electromyography is a methodology that can provide an indirect measure of muscle function occurring below the skin and soft tissue. The activation and intensity of muscular effort, characterised by the number of simultaneously recruited motor units, can be obtained by analysing the myoelectric signal that passes through the muscles and tissues and reaches the surface.

The knowledge of the significant factors of the motor units, such as the size of the muscles, the state of the motor units and the type of fibres composing them, are important for a correct interpretation of the EMG of the different muscles.

In order to understand EMG, muscle fibre activity must be assessed. As seen above, muscular excitation occurs when the neurons send, through the axons, an electrical signal that spreads through the muscle fibre at the same speed (2-5 m/sec) allowing the simultaneous contraction of all the sarcomeres. Muscle fibres contract according to the 'all-or-nothing' rule: if the force generating the contraction is above a certain threshold, there is an EMG signal.

The EMG is a recording that includes the asynchronous activity of electrical waves (action potentials) and varies in amplitude and duration as the distances of the muscle fibres from the electrode are different and the length of the axon varies according to the type of muscle.

Two main pieces of information can be obtained from the electromyographic trace: the duration and intensity of muscle activation. The duration can be obtained directly from the EMG signal, whereas the force and its intensity require processing of this signal. In particular, this is referred to as quantification and normalisation.

To be able to analyse an electromyographic recording, raw or processed, one can proceed with the analysis of the activation times (or bursts) of the muscles. The start and end time of the muscle activity interval is subjective, as a time window is taken that is useful for the analysis required. The duration is also influenced by the choice of EMG activity bursts.

Quantification allows the EMG trace to be processed in order to transform it into numerical values so that its relative intensity can be assessed. Quantization can be done either manually, but is less precise and accurate, or by means of a computer that allows for 100% repeatability.

Computerised quantization is done by digital sampling, rectification and data integration. The speed at which digitisation takes place is important because it should be fast enough to adequately reproduce the signal. Rectification allows all negative signals to be transposed into positive signals in order to prevent them from cancelling each other out. Integration, on the

other hand, allows the digitised and rectified EMG signals to be summed over an appropriate time interval in order to assess the clinical function of interest. Quantified EMG can be expressed as an absolute value (millivolts) or as a percentage with respect to a standard normalisation.

Normalisation is indispensable when comparing the intensity between two muscles, as two successive recordings with different placements do not produce the same quantitative data even if they took place with correct positioning of the electrodes. It is essential to correct the differences generated by the electrodes in the number and arrangement of motor units. It is performed by treating the acquired functional data as a proportion of a reference value generated with the same electrode. For example, for patients with normal nerve control, the reference could be the acquisition of maximal effort. In this way, it is possible to identify the real intensity of the muscular force required to walk or to perform all other functions [94].

6.1.1 EMG RECORDING INSTRUMENTATION

The quality and cleanliness of the EMG signal depends not only on the muscle intensity, but also on the instrumentation used for its acquisition. In particular, the type of electrodes, signal amplification and filtering techniques, signal transmission and recording system must be considered.

Myoelectric signals pass through both local muscle and adjacent soft tissue and can be recorded using three types of electrodes: needle, wire and surface. Surface electrodes consist of two metal discs placed directly on the skin, each with a cable connected to the amplifier. The most used are concave silver/silver chloride (Ag/AgCl) discs. This type of material provides a stable interface between the skin and the electrode by reducing polarisation, while the concavity contains a gel that increases conduction. For better signal reception, the patient's skin is prepared by removing dead cells using alcohol and abrasive sponges, and hair is also removed. Specifically, active surface electrodes are easy to apply and have internal amplifiers and an integrated circuit such that an optimal impedance is provided, producing a clear signal.

Wire or needle electrodes, on the other hand, make it possible to directly record the muscle activity of a specific muscle as they are inserted directly into it. The most used material is Nickel/Chromium alloy covered with Nylon. But their high flexibility makes them difficult to apply and consequently their stability is impaired.

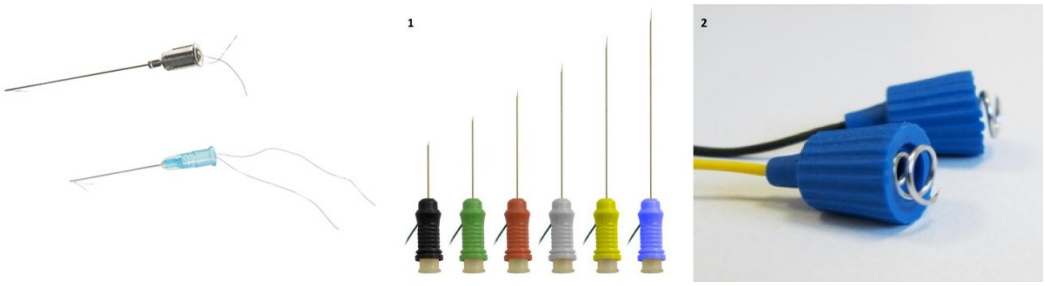


Figure 17: Needle electrodes. [95]

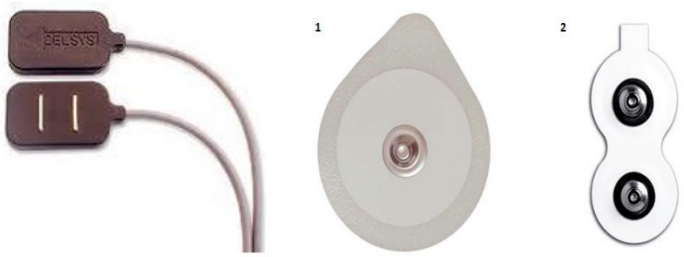


Figure 18: Surface electrodes. [95]

It can therefore be stated that: surface electrodes are associated with greater comfort due to their direct application on the skin, while wire electrodes are more selective.

The raw EMG is represented by the simultaneous action of several muscles with respect to the one under examination ('cross talk'), but by filtering it, it is possible to isolate the EMG data of the target muscle. In particular, the ability to differentiate between muscles depends on the frequency content: passing the signal through different tissues lowers the frequency content, as higher frequencies are attenuated by the tissues acting as low-pass filters, producing a different EMG trace for wire and surface electrodes. It is therefore important to define the use of each electrode: surface electrodes should be used to study a group of muscles, as opposed to wire electrodes used whenever there is a need to accurately identify muscle action.

In addition, EMG signals have frequencies that are too low to be used directly after their acquisition, so they need to be amplified with a differential amplifier to reduce signal interference and to have an impedance (1 Mohm) that can pick up low-level EMG signals. In addition, the signal must be filtered to eliminate soft tissue motion artefacts and electrical noise [94].

6.1.2 EMG DATA PROCESSING

For the study of the electromyographic signal, it is important to identify the parameters that characterize it in order to provide information about the functional status of the muscle under investigation.

As anticipated, the signal obtained from the electromyograph is a raw signal that provides only the activation times of a muscle. The signal must be filtered with a band-pass filter that cuts the frequency out of the 10-450 Hz range, since for frequencies between 50-60 Hz the signal is disturbed by background signals (skin potential) while frequencies above 450 Hz are not generated by motor units.

The signal can now be used for further processing. A frequently used operation is signal rectification: all negative frequencies are converted to positive, that is, the absolute value of the signal is calculated.

At this point, parameters for activation time (on and off), duration, peak envelope and fatigue indices can be obtained.

The activation and deactivation intervals of a muscle can be determined by filtering the signal by filter removing heartbeat, notch filter for 50 Hz, band-pass filtered with a double fifth-order Butterworth filter and full wave rectified. The cut-off frequencies varied from 5 to 15 Hz for the high-pass filter, and from 450 to 495 Hz for the low-pass filter. A double-threshold statistical detector proposed by Bonato [110] was applied. Background noise was estimated for each signal based on the interval of the subject's static standing. Only activation intervals longer than 30 ms were accepted. The values of duration of muscle activity and the onset and offset of muscle activity intervals were detected for each gait cycle. From here the activation duration can be calculated by making a difference between activation and deactivation.

The envelope was computed by low-pass filtering the signals with a 4th order Butterworth filter and a cut off frequency of 5 Hz as in [109].

The following values were derived for the analysis of muscle fatigue: Dimitrov Index (FI), Mean Frequency (MNF) and Root Mean Square(RMS).

In the following paper, the Dimitrov Index, for each repetition n, was calculated using the following formula:

$$FI_{nsm} = \frac{\int_{F_1}^{F_2} f^{-1} * PS(f) * df}{\int_{F_1}^{F_2} f^{5} * PS(f) * df}$$

Where PS(f) is the power spectrum calculated using the Fourier transform, F_1 and F_2 are 10 Hz and 450 Hz, respectively.

The resulting percent fatigue index is expressed as follows:

$$\frac{FI_{n_{nsm}}}{FI_{1_{nsm}}} * 100$$

Where n denotes the number of the repetition under consideration. In this way it is possible evaluate the percentage change in the parameter with each repetition, and the fatigue manifestation can be reflected in the percentage increase in FI_{nsm}.

Mean frequency is defined as the first-order spectral ratio and zero-order spectral moment:

$$FI_{nsm} = \frac{\int_{F_1}^{F_2} f * PS(f) * df}{\int_{F_1}^{F_2} PS(f) * df}$$

While Root Mean square (RMS) is a definition of signal amplitude is defined as:

$$x_{RMS} = \sqrt{\frac{1}{T} * \int_0^T x^2(t) dt}$$

which is the square root of the average signal strength over a given period.

According to the literature, muscle fatigue is ascertained by a significant increase in the amplitude of the EMG signal and a significant decrease in the frequency spectrum [111].

6.1.3 EMG INTERPRETATION

In order to determine the functional effectiveness of muscle action, it is necessary to properly interpret muscle activation in terms of duration and/or intensity.

The duration of muscular action (or timing of activation) in gait can be identified by means of three different scales: the stride cycle, the stance and swing periods and the functional phases that allow for a more correct functional interpretation.

The EMG signal has peaks with different amplitudes related to the different levels of force a muscle possesses. In fact, when there is a more intense muscle force, it means that more

motor units are recruited and the EMG recording becomes larger and denser. Therefore, quantification and normalisation are necessary to compare force intensity during different muscle activities.

EMG cannot provide the actual force of each muscle, it only identifies the magnitude of that force. What determines it is the type and speed of contraction and the length of the muscle fibres. Muscle force varies simultaneously with changes in the actin and myosin bridges and is the sum of the sarcomere force and the tension of the fibrous connective tissue.

During gait, all three forms of contraction (isometric, eccentric and concentric) are present: deceleration of the limb during the stance phase is favoured by eccentric concentrations, while peak muscle activity is isometric. The advancement of the limb during the swing is favoured by concentric contractions. It must be emphasised, that motor units can be recruited in different ways even during the same activity.

It can therefore be said that the relationship between EMG and force changes continuously, resulting in a variable muscle force without changing the number of active motor units. The electromechanical delay, i.e. the time with which the electrical response precedes the mechanical reaction, must also be considered. And muscle synergies are also a problem because they make it impossible to precisely assign the measured moment to a specific muscle. But it is possible, through indirect measurements, to have an indication of the force [94].

6.1.4 THE PATHOLOGICAL PATH

Pathologies that alter motor functions, specifically walking, involve four main functional changes: deformity, muscle weakness, altered control and pain. Knowing these characteristics means knowing the compensatory actions that are naturally performed by our organism when a function stop being exercised.

Deformity occurs when normal posture and motor control are impeded, hindering adequate passive mobility. One of the most frequent causes is retraction, i.e. a change in the structure of fibrous connective tissue, ligaments and joint capsules. A distinction is made between an elastic retraction where forced manual lengthening is required: strong tractions are not exerted during walking and tissue stretching may occur; and a rigid retraction where any type of lengthening is prevented and muscle activity is increased to stabilise the knee, thus increasing compensation actions.

The patient may not be able to exert the force required to perform the functions required for walking. If they are only affected by muscle weakness, one can act on the muscle activation pattern in order to avoid compensation phenomena. If, on the other hand, the muscle impairment is extensive or there is retraction in the muscles involved in the basic compensations, the joints become unstable.

If proprioceptive damage (loss of sensation) is present, the patient is no longer able to know the position of the limbs in space. Three degrees are generally identified: absent, impaired or normal.

Pain results from tension developing in the tissues. This condition can alter gait through deformity and muscle weakness. Deformity occurs when a painful limb assumes a position independently, resulting in muscle weakness due to decreased utilisation of the injured area.

Patients with a CNS lesion, which causes spastic paralysis, develop five motor deficits. The basic reaction is an excessive stretch response (spasticity), impairment of selective control, activation of primitive locomotion patterns, change of motor patterns and alteration of proprioception. In addition, muscle control is altered by limb position and body alignment. Spastic gait is caused by cerebral palsy, stroke, cerebral and incomplete spinal cord injury and multiple sclerosis.

Spasticity modifies the eccentric contraction during stance and is evidenced by a short muscle contraction (clonus) during a rapid stretch and a sustained muscle action during a slow stretch.

Figure 19: Response of a spastic muscle to stretching (EMG). (a). rapid stretching elicits a clonus. (b). slow stretching elicits a sustained muscle action. [94]

In this condition, the patient loses the ability to control muscle intensity: the action of any muscle may be prolonged or interrupted, premature or delayed, continuous or absent.

Only patients with a picture of medium severity are able to adapt to the injury: hemiplegia, for example, has a better chance since it involves only one side of the body, as does paraplegia; while quadriplegia is the most disabling injury.

6.1.4.1 EMG ANALYSIS OF THE PATHALOGICAL PATH

During the gait analysis of an EMG tracing, errors in neurological control, muscle weakness, voluntary compensations and forced postures can be detected. As a result, both duration and intensity may be altered in a single phase or the entire gait cycle.

Abnormal activity is classified through seven levels: premature, prolonged, continuous, delayed, interrupted, absent and out-of-phase.

EMG Activation Errors	
Deviation	**Definition**
Premature	The action starts before normal onset
Prolonged	Action continues beyond normal cessation time
Continuous	Uninterrupted EMG for 90% or more of step cycle
Abbreviated	Early cessation of EMG
Delayed	Later than normal onset
Absent	EMG of insufficient amplitude or duration
Off-axis	Reversed periods of oscillation or stance

Table 4:Classification of abnormal activity of EMG for pathological path [94].

Pathological function, on the other hand, is identified as: excessive, inadequate or absent. The normal range is represented by the standard deviation above and below the normal mean. Excessive activity is verified by correlating the EMG amplitude with the muscle examination values. Generally, the EMG pattern is modified by clones in patients exhibiting spasticity and by enlargement of motor units in lower motor neuron pathology.

Intensity-related errors	
Deviation	**Definition**
Excessive	EMG value greater than normal range
Insufficient	EMG value less than normal range
Absent	Insufficient EMG to identify functional significance

Table 5: Classification of pathological path [94].

7 MATERIALS AND METHODS

The study was carried out in collaboration with the Centro Medico di Fisioterapia in Padua, the VIKTOR Physiotherapy Centre in Dalmine, Bergamo, and the BiomovLab Laboratory of Movement Bioengineering at the University of Padua. Due to problems with patient attendance at the Padua centre, the data used were provided by the VIKTOR Physiotherapy Centre Physio Lab in Dalmine.

The objective of the present study is to evaluate the functioning of the VIKTOR method through an analysis of electromyographic data before and after treatment with the VIK16 workstation. Specifically, EMG data were analysed using SMARTAnalyzer software and subsequently processed using MATLAB codes provided by the Biomov laboratory in Padua and integrated and developed by the undersigned.

All patients had muscles that were different from each other but still concordant to those present in healthy subjects, so processing was done by comparing individual muscles in the three different cases: muscles of healthy subjects, muscles of patients before and after treatment.

7.1 SUBJECTS

The data provided by the Dalmine Centre included 10 patients with different types of neurological disease and trauma, mainly plague, and 8 healthy subjects for the control group. For the following study, however, only 6 patients were considered due to the presence of erroneous files and/or with a length of EMG tracing too small to be analysed (subj_3, subj_5, subj_9 and subj_10 were excluded). One subject in the control group (healthy_3) was also excluded because he had a different muscle than all the others.

The parameters for age, BMI and gender of the control group are shown in Table 6, while those for age, BMI, gender, pathology type and treatment duration of the pathological subjects are shown in Table 7.

HEALTHY	AGE	BMI	GENDER
HEALTHY_1	47	25.4	Male
HEALTHY_2	35	23.3	Male
HEALTHY_4	51	24.2	Female

HEALTHY_5	25	20.5	Male
HEALTHY_6	53	26.1	Male
HEALTHY_7	47	23.1	Male
HEALTHY_8	58	22.3	Female

Table 6: Age and BMI for the control group.

PATIENT	AGE	BMI	GENDER	PATHOLOGY	YEAR TREATMENT
SUBJ_1	54	24.2	Male	Multiple Sclerosis	2021-2023
SUBJ_2	66-67	24.2	Male	Hemiparesis SX	2019-2020
SUBJ_4	59	25.8	Male	Tetra paresis	2018-2019
SUBJ_6	82-84	23.1	Male	Hemiparesis DX	2019
SUBJ_7	19-23	22.0	Female	Hemiparesis DX	2019-2022
SUBJ_8	33	21.3	Female	Tetra paresis	2018-2021

Table 7: Data patients considered for the study.

All muscles acquired, between control subjects and patients, are shown below and for ease of writing have been named with codes:

- BBCC: Biceps Brachii Caput Brevis;
- BBCL: Biceps Brachii Caput Longus;
- BFCL: Biceps Femoris Caput longus;
- DA: Deltoideus Anterior;
- DP: Deltoideus Posterior;
- ESL: Erector Spinae Longissimus;
- ED: Extensor Digitorum;
- FPR: Flexor Carpi Radialis;
- GAL: Gastrocnemius Laterlis;
- GM: Gluteus Maximus;
- RF: Rectus Femoris;
- TA: Tibialis Anterior;
- TD: Trapezius Descendens;
- TBCLA: Triceps Brachii Caput Lateralis;
- TBCLU: Triceps Brachii Caput Longus;
- VL: Vastus Lateralis;
- EPRL: Extensor Carpi Radialis Longus;
- OEA: Obliquus Externus Abdominis;
- VM: Vastus Medialis;

- GME: Gluteus Medius;
- GAM: Gastrocnemius Medialis;
- TBL: Tensor Fasciae Latae.

The prefixes R or L in front of the abbreviations were used to specify the right and left muscles.

7.2 EQUIPMENT

7.2.1 HARDWARE

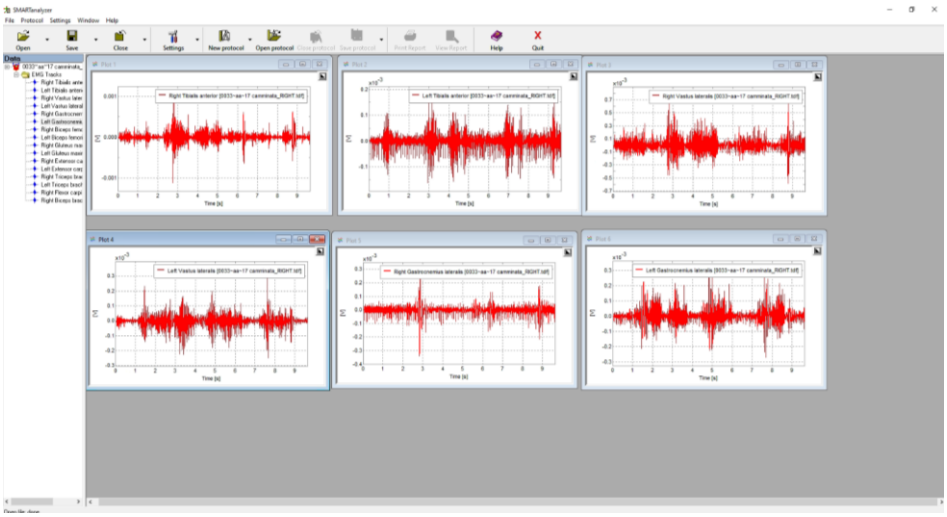
For the acquisition of the electromyographic trace, electrodes were placed directly on the patient's skin, previously shaved from the presence of any hair and cleaned for better adherence. Specifically, FIAB electrodes were used, disposable electrodes that already contain gel integrated within them in order to improve signal acquisition.

Figure 20: FIAB Electrodes used for the acquisition of EMG.[101]

7.2.2 SOFTWARE

The software used for data analysis were as follows:

- SMARTAnalyzer: a software that allows biomechanical analysis of movement from 3D kinematic data and from force platforms, electromyographs or other devices. It provides a tool to generate all useful data for a complete motor gesture analysis. It was used for an initial analysis of EMG data in order to identify a time window of analysis that was the same for all subjects (2 to 7 s). It also allowed the identification of any errors present in the .tdf files related to the EMG acquisitions. [102]



– MATLAB: a programming and numerical computing language that enables the development of algorithms and models useful for processing data from multiple types of files and is capable of returning processed output files in the form of tables, graphs and trends. Its layout allows the 'Current Folder', where the current working folder is specified, the 'Workspace' where variables created or imported from files are displayed, the 'Command Window' that allows commands to be entered from the command line (indicated by the >> prompt), and the 'Editor' sheet that allows code to be written on the same window [103].

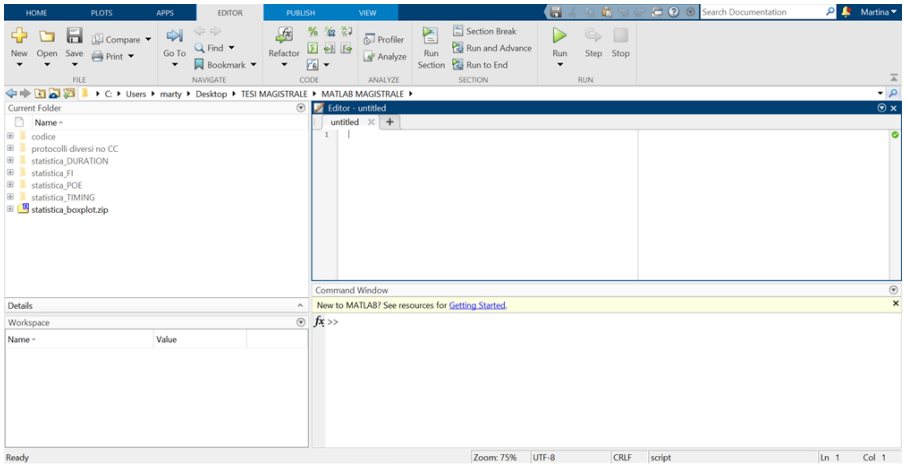


Figure 21: Matlab home screen.

– Microsoft Excel: a program used for creating and managing spreadsheets. It allows you to perform calculations such as addition, subtraction, division, multiplication and many others. It also allows you to construct diagrams and statistical charts from the data selected in the spreadsheet. It has been used for saving all data processed through Matlab codes and for creating bar charts for displaying percentage fatigue [104].

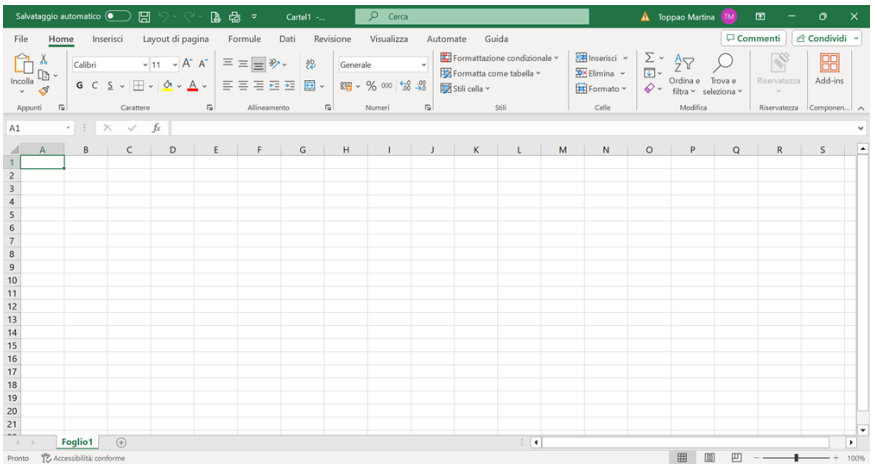


Figure 22: Excel home screen.

7.3 DATA ACQUSITION

7.3.1 PATIENT'S PROTOCOL

Data were acquired at the VIKTOR Physio Lab Centre, and all patients underwent two acquisition sessions: before and after treatment through VIK16. Each patient had an individualized FES protocol based on the type of disability and therefore the exercises performed, chosen from the 50 programs offered by the machine, differed between patients. The muscles of the whole body were acquired, focusing, however, on those with greater dysfunction: patients with a right hemiparesis presented a greater number of electrodes on the right side, vice versa for patients with a left hemiparesis, which presented a greater concentration of electrodes on the left side. In contrast, for quadriplegic patients, there is an almost equal distribution of electrodes between the right and left.

PATIENT	EXERCISES PERFORMED	MUSCLES ACQUIRED PRE	MUSCLES ACQUIRED POST
SUBJ_1	1-4-5-1-32-35-39-45-46-50	RDA, LDA, RBBCL, RTBCLU, RFPR, RED, RESL, LESL, RGM, LGM, RBFCL, LBFCL, RVL, RTA, LTA, RGAL	RDA, LDA, RBBCL, RTBCLU, RFPR, RED, RESL, LESL, RGM, LGM, RBFCL, LBFCL, RVL, RTA, LTA, RGAL

SUBJ_2	1-2-4-5-20-22-35-36-50	LTD, RDA, LDA, LDP, LBBCL, LFPR, LED, LESL, LGM, RGM, LVL, RVL, LBFCL, LTA, RTA, LGAL	LTD, RDA, LDA, LDP, LBBCL, LFPR, LED, LESL, LGM, RGM, LVL, RVL, LBFCL, LTA, RTA, LGAL
SUBJ_4	1-2-3-4-5-11-15-18-43-46-50	RTA, LTA, RVL, LVL, RGAL, LGAL, RBFCL, LBFCL, RGM, LGM, REPRL, LEPRL, RTBCLA, LTBCLA, RFPR, RBBCL	RTA, LTA, RVL, LVL, RGAL, LGAL, RBFCL, LBFCL, RGM, LGM, REPRL, LEPRL, RTBCLU, LTBCLU, RFPR, RBBCL
SUBJ_6	1-4-5-7-16-34-38-46-50	RTA, LTA, RGAL, LGAL, RVL, LVL, RRF, LRF, RBFCL, LBFCL, RGM, LGM, RESL, LESL, ROEA, LOEA	RTA, LTA, RGAL, LGAL, RVL, LVL, RRF, LRF, RBFCL, LBFCL, RGM, LGM, RESL, LESL, ROEA, LOEA
SUBJ_7	1-2-3-4-5-16-18-22-30-32-34-35-39-50	RTA, LTA, RGAL, LGAL, RBFCL, LBFCL, RVM, RRF, RGM, LGM, RGME, LGME, ROEA, LOEA, RESL, LESL	RTA, LTA, RGAL, LGAL, RBFCL, LBFCL, RVM, RRF, RGM, LGM, RGME, LGME, ROEA, LOEA, RESL, LESL
SUBJ_8	1-4-5-6-11-21-25-35-50-22	RTA, LTA, RVL, LVL, RGAL, LGAL, RBFCL, LBFCL, RGM, LGM, REPRL, LEPRL, RTBCLA, LTBCLA, RFPR, RBBCL	RTA, LTA, RGAL, LGAL, RGAM, RRF, LRF, RTBL, RGM, LGM, RESL, LESL, RBBCL, RTBCLU, LDA, RDA

Table 8: Number of patients with respective exercises performed during treatment and muscles gained before and after.

All electrodes were placed according to SENIAM [105] guidelines. The duration of each session was approximately 45 minutes, and patients performed a different number of sessions from each other (some participated in treatment for several years as well, Table 7). Specifications on electrical stimulation parameters were selected according to each patient's functional capacity. Prior to treatment or at any rate at the time of initiation of the treatment session, the sensitivity threshold of each muscle group was measured, i.e., the level of current that could be delivered for the manifestation of pronounced muscle contraction to occur

without the appearance of pain. Average data for the treatments performed, such as frequency, pulse duration, number of sessions, cycles and sensitivity, are shown in Table 9.

PATIENT	FREQUENCY (Hz)	IMPULSE DURATION (µS)	SENSIBILITY (mA)	TOTAL SESSION (SESSION A WEEK)	TOTAL CYCLE (CYCLE A SESSION)
SUBJ_1	100	200	20	10 (5)	400 (40)
SUBJ_2	100	200	15	42 (1)	3600 (90)
SUBJ_4	100	200	16	45 (2)	2000 (45)
SUBJ_6	100	200	20	40 (2)	2000 (50)
SUBJ7	100	200	20	276 (2/3)	17000 (70)
SUBJ_8	100	200	15	52 (1)	3200 (50)

Table 9: Average data for treatments performed.

7.3.2 CONTROL GROUP PROTOCL

Subjects in the control group followed an acquisition protocol in line with that of the patients, so that they were able to match the muscles recorded and the exercises performed. Specifically, 16 muscles were recorded for the right side and 16 for the left side in order to be able to match the corresponding hemiparesis, as previous studies have confirmed the equality of muscle synergies in movements performed by healthy people [106].

Muscles acquired are: RBBCC, LBBCC, RBBCL, LBBCL, RBFCL, LBFCL, RDA, LDA, RDP, LDP, RESL, LESL, RED, LED, RFPR, LFPR, RGAL, LGAL, RGM, LGM, RRF, LRF, RTA, LTA, RTD, LTD, RTBCLA, LTBCLA, RTBCLU, LTBCLU, RVL, LVL.

7.4 DATA ANALYSIS

In order to evaluate the functioning of the method, only the gait, corresponding to the 50-program implemented in VIK16, was analysed. In addition, due to the diversity of muscles acquired in different patients, only those in agreement with the muscles of the subjects belonging to the control group were considered, including those with no correspondence between before and after treatment.

That is, the following 32 muscles were considered: RBBCC, LBBCC, RBBCL, LBBCL, RBFCL, LBFCL, RDA, LDA, RDP, LDP, RESL, LESL, RED, LED, RFPR, LFPR, RGAL, LGAL, RGM, RRM, RRF, LRF, RTA, LTA, RTD, RTDL, LBCLA, LTBCLA, RTBCLU, LTBCLU, RVL, LVL.

Initially, the Smart Analyzer software was used, which enabled the visualization of signal graphs in voltage [V] versus time [s]. This allowed the identification of a time window, from 2 to 7 s, concordant to all muscles.

Data processing began using a Matlab code that required as input two .tdf files, one related to the right and one related to the left muscles, and the time window considered. This code was run for the EMG recording files of the control group subjects and patients before and after treatment. The code resulted in a file called output.mat, a 1x2 structure containing all the parameters related to the electromyographic tracing divided between right and left:

- `trialname`: contains name of the .tdf files given as input;
- `side`: specifies which muscles we are considering, right or left;
- `labels`: vector grouping all muscle names (1x16 cells);
- `raw_signal`: contains, for each muscle, all the values obtained from the raw file (1x16 cells);
- `envelopeParam`: structure that contains information about the signal envelope. Specifically we find: `maxEmgValue` (1x16 cell), `maxEmgPosition` (1x16 cell), `envelope_signals` (1x16 cell) and `maxEmgNormValue` (1x16 cell);
- `filtered_signals`: contains the filtered EMG signals;
- `noise_signals`: contains the noise signals;
- `instants`: contains the considered time instants (1x16 cells);
- `stParameters`: structure containing all gait-related parameters, such as `gaitSpeed`, `strideLength`, `strideTime`;
- `detecParameters`: structure containing the parameters related to detection, such as threshold Th, signal-to-noise ratio SNR and others;
- `onoff`: structure containing information about the activation and deactivation of muscles;
- `activity_quantification`: structure containing all values related to activity quantification, i.e., `maxContraction`, `normalizedEnv`, `poe`, `ppoe`, `ppoe_gaitpercentage`.

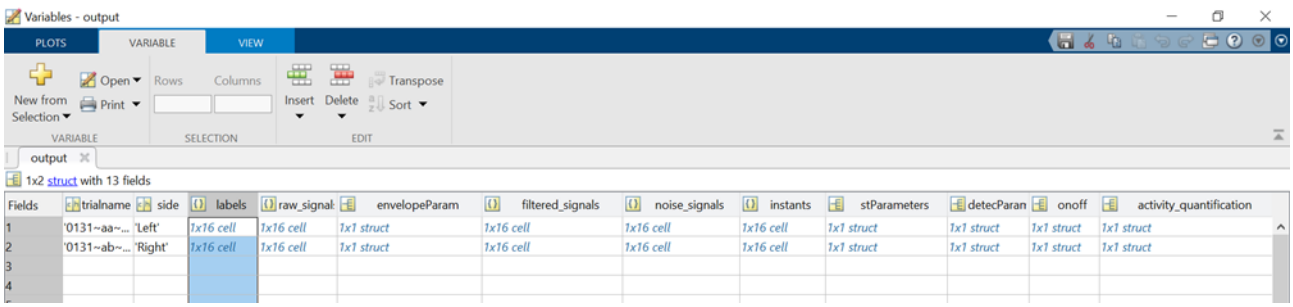


Figure 23: File output.mat.

At the end of the processing, two folders containing graphs related to the extrapolated parameters were obtained. These folders were given as input to a matlab code that allowed obtaining Excel (.xlsx) files containing all the data obtained in the form of spreadsheets. Specifically, the following files were obtained for left and right, pre and post:

- BurstParameters: values related to envelope peaks and their positions;
- Durations: values related to the durations of the muscles;
- EnvelopeNormalized: values of normalized envelopes;
- envelopeNormalizedParameter: values of normalized envelopes in the form of percentages;
- Timing: activation and deactivation times of muscles;
- UsedInstants_inFrames: instants of time considered.

Next, from the output.mat file obtained from the previous code, a Matlab code capable of extracting the maximum value of the signal envelopes was developed.

```
data_LEFT=output(1).envelopeParam.envelope_signals;
data_RIGHT=output(2).envelopeParam.envelope_signals;
```

This was saved in an Excel file where the maximum value was paired with the corresponding muscle.

Later, an additional Matlab code was used to extract the values related to muscle fatigue: Dimitrov Index (FI), Root Mean Square (RMS), Mean Frequency (MNF). The percentage values of these variables were obtained from the regression lines, output of the Matlab code under consideration, by plotting the frequency on the walk cycle under consideration that: fatigue is present if the line of FI and RMS has an increasing trend ($m>0$) and if the line of MNF has a decreasing trend ($m<0$).

Percent fatigue (FI%) was calculated for muscles that were in common with control subjects and had a match between before and after, taking into account that the percentage for control

subjects was performed on a total of seven subjects, while the percentage for patients was performed with respect to the cohort of patients who had that specific muscle. In Table 11 we can see which patients were acquired for a given muscle.

MUSCLES	NUMBER OF PATIENTS BEFORE (PATIENTS)	NUMBER OF PATIENTS AFTER (PATIENTS)
RBBCC	0	0
LBBCC	0	0
RBBCL	3 (1, 4, 8)	3 (1, 4, 8)
LBBCL	1 (2)	1 (2)
RBFCL	5 (1, 4, 6, 7, 8)	4 (1, 4, 6, 7)
LBFCL	6 (1, 2, 4, 6, 7, 8)	5 (1, 2, 4, 6, 7)
RDA	1 (1)	2 (1, 8)
LDA	2 (1, 2)	3 (1, 2, 8)
RDP	0	0
LDP	1 (2)	1 (2)
RESL	3 (1, 6, 7)	4 (1, 6, 7, 8)
LESL	4 (1, 2, 6, 7)	5 (1, 2, 6, 7, 8)
RED	1 (1)	1 (1)
LED	1 (2)	1 (2)
RFPR	3 (1, 4, 8)	2 (1, 4)
LFPR	1 (2)	1 (2)
RGAL	5 (1, 4, 6, 7, 8)	5 (1, 4, 6, 7, 8)
LGAL	5 (2, 4, 6, 7, 8)	5 (2, 4, 6, 7, 8)
RGM	6 (1, 2, 4, 6, 7, 8)	6 (1, 2, 4, 6, 7, 8)
LGM	6 (1, 2, 4, 6, 7, 8)	6 (1, 2, 4, 6, 7, 8)
RRF	2 (6, 7)	3 (6, 7, 8)
LRF	1 (6)	2 (6, 8)
RTA	6 (1, 2, 4, 6, 7, 8)	6 (1, 2, 4, 6, 7, 8)
LTA	6 (1, 2, 4, 6, 7, 8)	6 (1, 2, 4, 6, 7, 8)
RTD	0	0

LTD	1 (2)	1 (2)
RTBCLA	2 (4, 8)	0
LTBCLA	2 (4, 8)	0
RTBCLU	1 (1)	3 (1, 4, 8)
LTBCLU	0	1 (4)
RVL	5 (1, 2, 4, 6, 8)	4 (1, 2, 4, 6)
LVL	4 (2, 4, 6, 8)	3 (2, 4, 6)

Table 10: Number of patients acquired per single muscle.

It should be specified that: in SUBJ_4 in the acquisition before treatment the RTBCLA and LTBCLA muscles were acquired, after treatment instead we find the RTBCLU and LTBCLU muscles; in SUBJ_8 the muscles acquired before treatment were RVL, LVL, RBFCL, LBFCL, REPRL, LEPRL, RTBCLA, LTBCLA, RFPR, after treatment instead we find the RGAM, RRF, LRF, RTBL, RESL, LESL, RTBCLU, LDA, RDA muscles. Finally, the LDA muscle of SUBJ_2 was excluded because it created problems in the first data processing.

7.5 STATISTICAL ANALYSIS

A statistical analysis was conducted for the variables obtained from the previous Matlab codes: Dimitrov Index (FI), Duration (Durations), Peak Envelope (POE), and Activation Times (Timing, ON and OFF).

Excel files were created separately for the variables just specified and separately for the values of the three cases: values of the healthy, values of the patients before treatment, and values of the patients after treatment.

The Wilcoxon Test, a nonparametric test commonly used for the two-sample localization problem and for detecting differences in median values, was implemented in Matlab for all four variables. It has two versions:

- the Wilcoxon Rank-sum test, used to compare two independent samples;
- the Wilcoxon Signed-rank test, used to compare two paired samples [107].

Specifically, the Wilcoxon Rank-sum test was used to compare healthy subjects' values with patients' values before and after treatment for each variable; while the Wilcoxon Signed-rank test was used to compare patients' values before and after treatment, as they were measurements performed on the same population.

The code allowed us to output the 'p_values' associated with the individual muscles resulting from the comparison between the two groups under test, i.e., the probability of observing by chance the given result or that the null hypothesis (medians are equal) is true, small values questioning the validity of the null hypothesis; and the 'h' value, which returns the result of the test: h=0 indicates that the null hypothesis cannot be rejected, h=1 indicates that the null hypothesis can be rejected.

The values of the four variables were then plotted using Matlab's `boxplot()` function where, for FI, DURATION, POE, data from healthy subjects were compared to those of patients before treatment, data from healthy subjects to data from patients after treatment, and data from patients before treatment to data after treatment. For the TIMING variable, on the other hand, all values of activation (ON) and deactivation (OFF) of a muscle for the three cases (healthy, patients before, patients after) were compared. In addition, an asterisk was placed where the difference between the groups was found to be statistically significant ($p\_value<0.05$).

8 RESULTS

The following section discusses the results obtained from the statistical analysis of the four variables found from the previous processing: Timing, Duration, Peak of Envelope and Index of Dimitrov. For the analysis of percent fatigue, all muscles concordant to the muscles of healthy subjects were considered, excluding those that did not show correspondence between before and after treatment for patients. For the analysis of timing, duration, and peak of envelope, all muscles concordant to the muscles of the healthy subjects were considered, including those without correspondence between before and after treatment, but only those for which there is correspondence between before and after are reported.

In light of the fact that not all muscles show correspondence between before and after treatment, of the 32 muscles analysed, only 25 were considered.

8.1 DIMITROV INDEX (FI) ANALYSIS

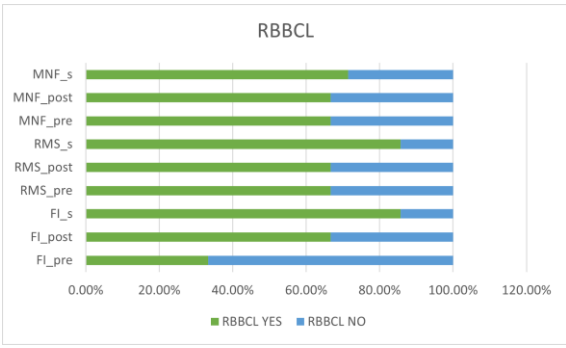
In the statistical analysis of the Dimitrov index, fatigue manifestations were evaluated, but no statistically significant differences were found. Therefore, the percentages for the presence or absence of fatigue on individual muscles were considered. The graphs for the boxplots are given at the queue of this paper (Chapter 12).

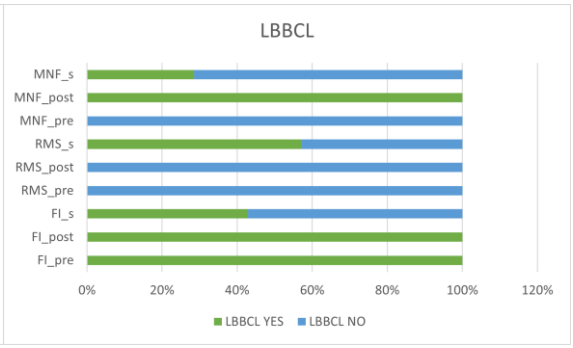
From the stacked bar graphs related to percent fatigue, made using an Excel spreadsheet, it can be seen that:

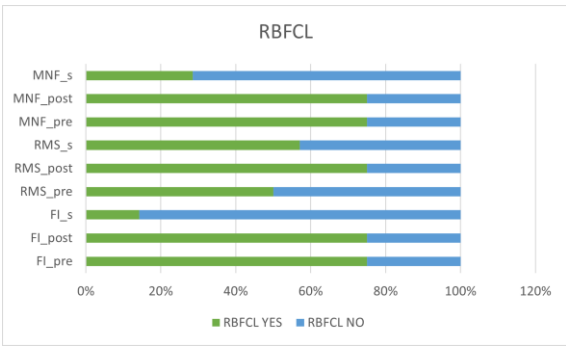
- in the muscles RBBCL, LBBCL, RBFCL, RDA, LDA, RGAL, LGAL, RGM, LGM, RTA, LTA, LTD, and LVL, fatigue manifestations were detected both before and after treatment.

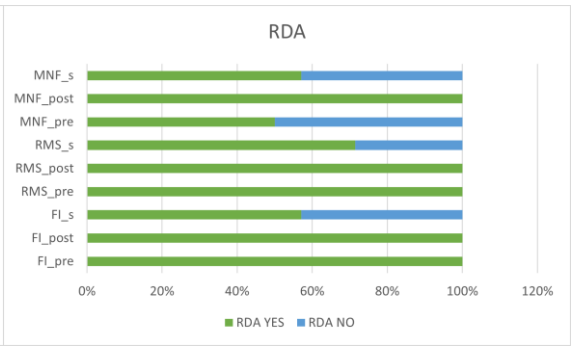

RBFCL
MNF_s
MNF_post
MNF_pre
RMS_s
RMS_post
RMS_pre
FI_s
FI_post
FI_pre
0%
20%
40%
60%
80%
100%
120%
RBFCL YES
RBFCL NO

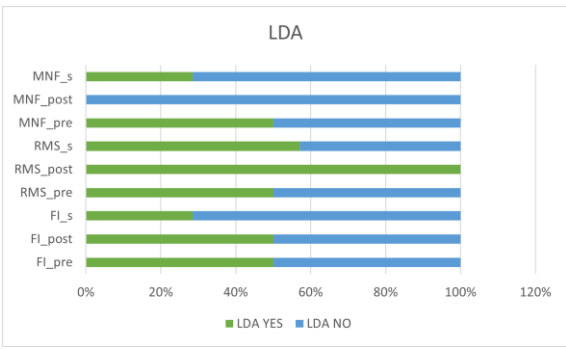
RDA
MNF_s
MNF_post
MNF_pre
RMS_s
RMS_post
RMS_pre
FI_s
FI_post
FI_pre
0%
20%
40%
60%
80%
100%
120%
RDA YES
RDA NO

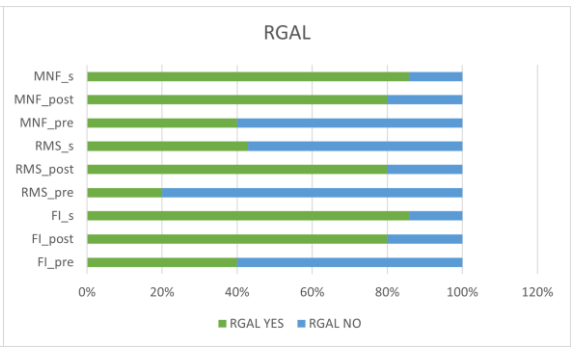

RBBCL
MNF_s
MNF_post
MNF_pre
RMS_s
RMS_post
RMS_pre
FI_s
FI_post
FI_pre
0.00%
20.00%
40.00%
60.00%
80.00%
100.00%
120.00%
RBBCL YES
RBBCL NO

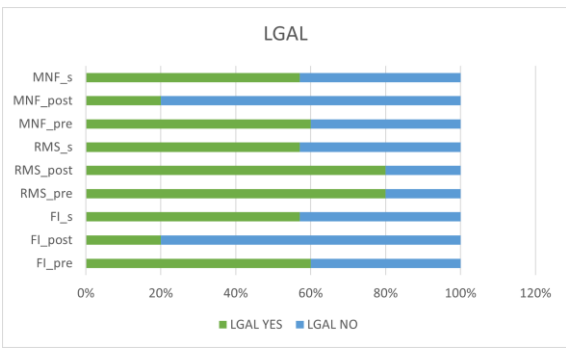

LBBCL
MNF_s
MNF_post
MNF_pre
RMS_s
RMS_post
RMS_pre
FI_s
FI_post
FI_pre
0%
20%
40%
60%
80%
100%
120%
LBBCL YES
LBBCL NO

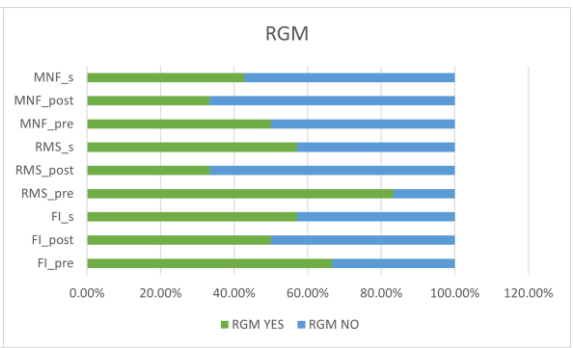

RBFCL
MNF_s
MNF_post
MNF_pre
RMS_s
RMS_post
RMS_pre
FI_s
FI_post
FI_pre
0%
20%
40%
60%
80%
100%
120%
RBFCL YES
RBFCL NO


RDA
MNF_s
MNF_post
MNF_pre
RMS_s
RMS_post
RMS_pre
FI_s
FI_post
FI_pre
0%
20%
40%
60%
80%
100%
120%
RDA YES
RDA NO


LDA
MNF_s
MNF_post
MNF_pre
RMS_s
RMS_post
RMS_pre
FI_s
FI_post
FI_pre
0%
20%
40%
60%
80%
100%
120%
LDA YES
LDA NO


RGAL
MNF_s
MNF_post
MNF_pre
RMS_s
RMS_post
RMS_pre
FI_s
FI_post
FI_pre
0%
20%
40%
60%
80%
100%
120%
RGAL YES
RGAL NO


LGAL
MNF_s
MNF_post
MNF_pre
RMS_s
RMS_post
RMS_pre
FI_s
FI_post
FI_pre
0%
20%
40%
60%
80%
100%
120%
LGAL YES
LGAL NO


RGM
MNF_s
MNF_post
MNF_pre
RMS_s
RMS_post
RMS_pre
FI_s
FI_post
FI_pre
0.00%
20.00%
40.00%
60.00%
80.00%
100.00%
120.00%
RGM YES
RGM NO

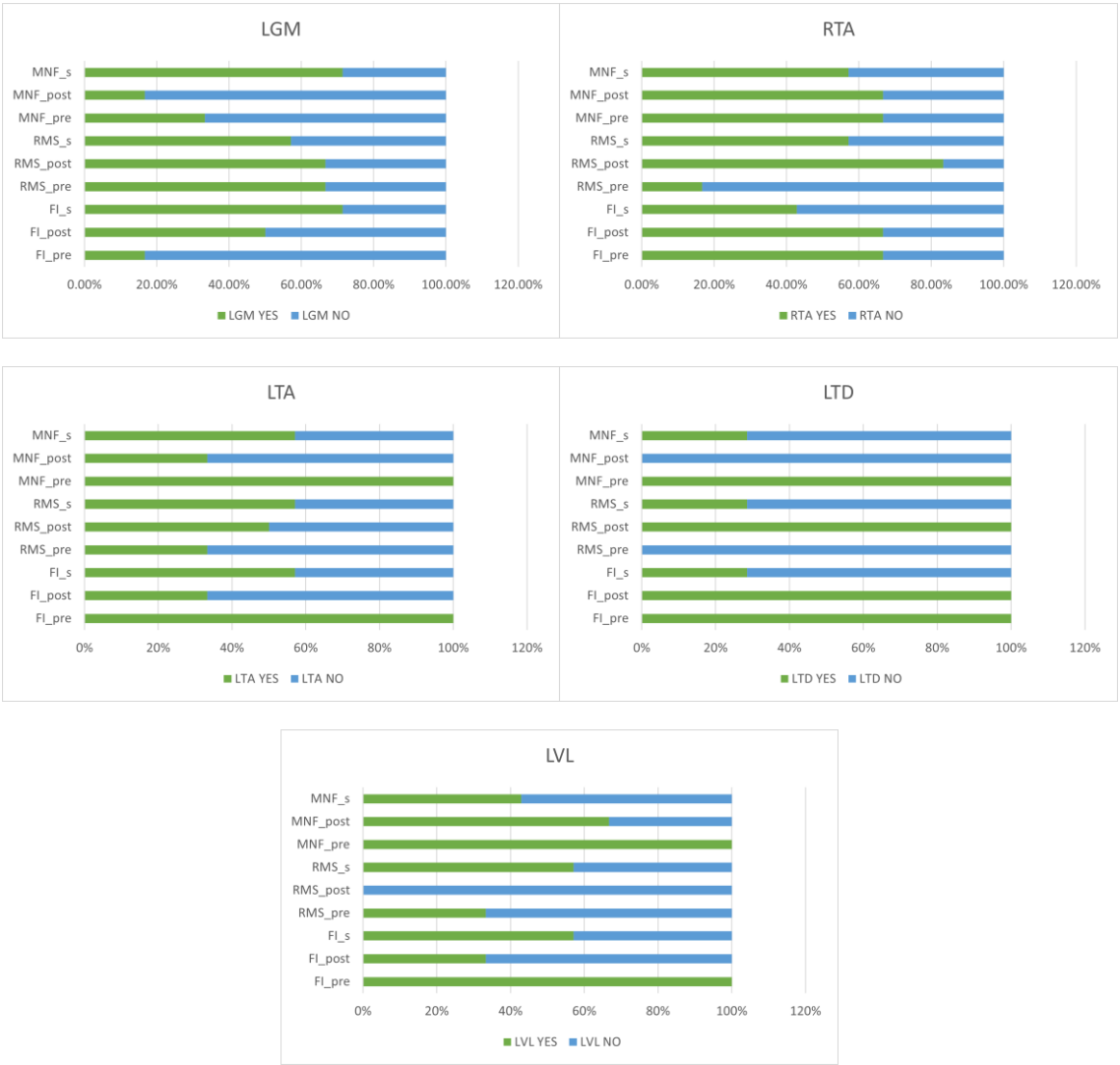


Figure 24: Muscles that shows fatigue before and after treatment.

– in LBFCL, LDP, RED, RESL, LESL, RFPR and RTBCLA muscles, fatigue manifestations were detected only before treatment.

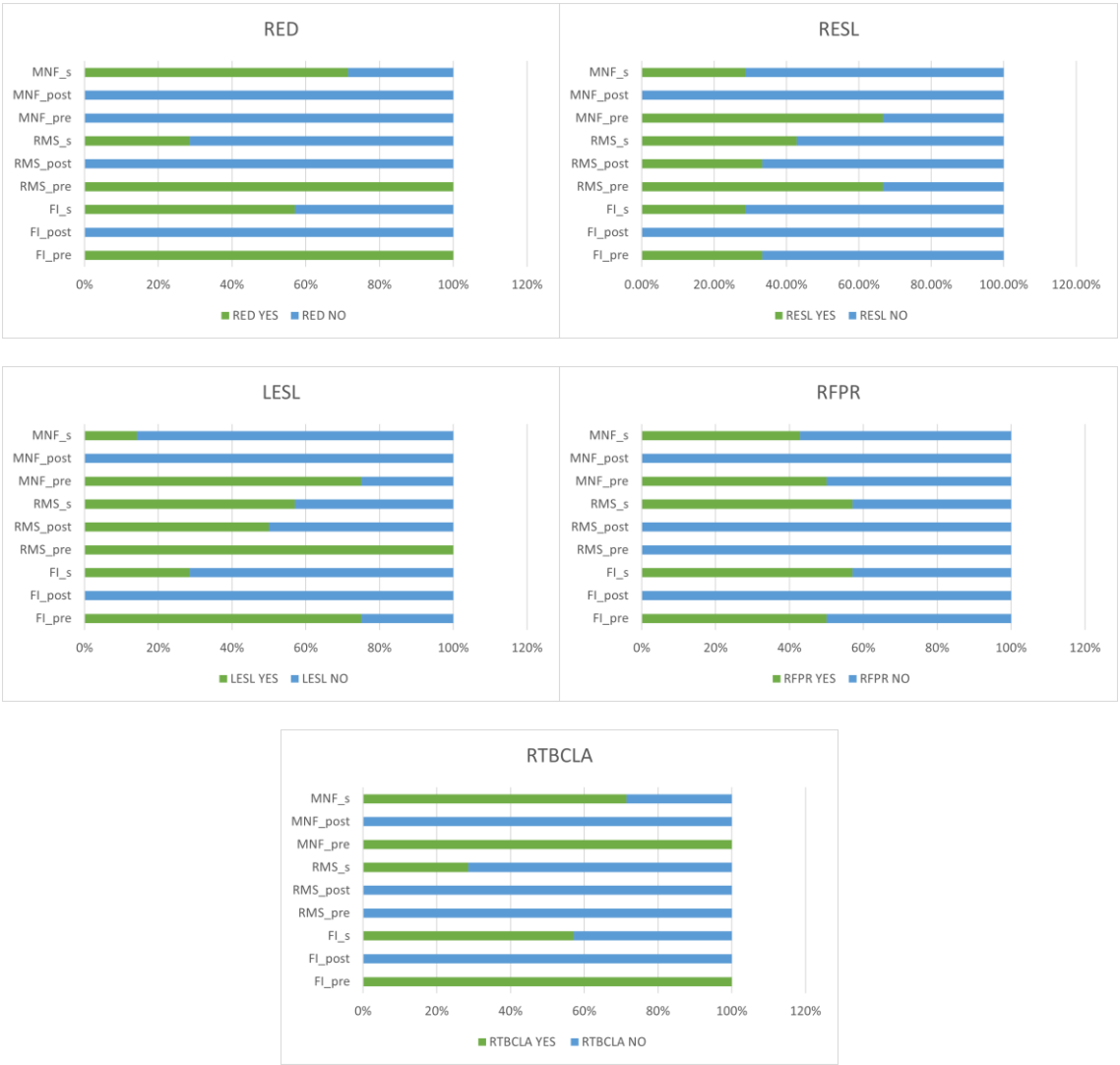


Figure 25: Muscles that shows fatigue only before treatment.

– in LED, LRF and RVL muscles, fatigue manifestations were detected only after treatment.

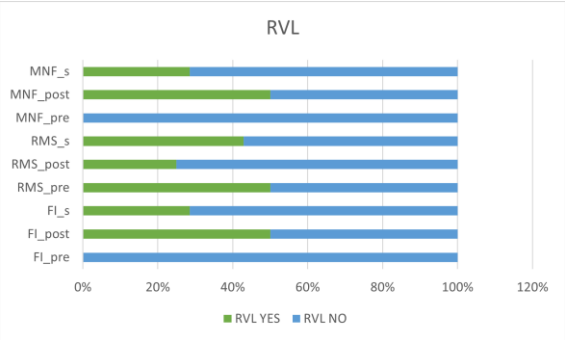


Figure 26:Muscles that shows fatigue only after treatment.

– in the LFPR, RRF, LTBCLA and RTBCLU muscles, no fatigue manifestations were detected.

Figure 27: muscles that show no fatigue.

8.2 DURATION ANALYSIS

In the duration analysis, the period of activation of each muscle was evaluated, and through the boxplots, made for displaying the statistics, statistically significant differences were observed. The duration values of healthy subjects (Hs) on the values of patients before treatment (BT), the values of healthy subjects on the values of patients after treatment (AT), and the values of patients before on the values of patients after treatment were plotted.

It was inferred that:

- in all 32 muscles, statistically significant differences were found between Hs and BT;
- in the muscles LBBCL, RBFCL, LBFCL, LDA, RDP, LDP, LESL, RED, LED, LFPR, RGAL, LGAL, LGM, LRF, LTA, RTBCLU, LTBCLU, LVL, RTD, LTD, LTBCLA statistically significant differences were detected between Hs and AT;
- no statistically significant differences were detected between BT and AT.

Comparison of the average values obtained, considering that higher values correspond to longer duration, shows that:

- in RBBCL, LDA, RED and RRF muscles, there are higher values in Hs than in BT, in BT than in Hs and in AT than in BT;
- in RBFCL and LFPR muscles, the values of Hs and BT are equal, are greater in AT than Hs and in AT than BT;
- in RDA muscle, are greater in Hs than in BT, in Hs than in AT while they are equal between BT and AT;
- in RGAL and LGAL muscles, are greater in BT than in Hs, lesser in AT than in Hs and in AT than in BT;
- in muscles RVL and LVL, are greater in BT than Hs, in AT than Hs and in AT than BT;
- in muscles LBBCL, RESL, LESL, RGM and LGM, are greater in BT than Hs, in AT than Hs and equal between BT and AT;
- in LBFCL, RFPR and LRF muscles, are equal between Hs, BT and AT;
- in muscles LDP, LED, RTBCLU and LTD, are greater in BT than Hs, in AT than Hs and in BT than AT;
- in RTA and LTA muscles, are found to be greater in Hs than in BT, equal between Hs and AT and greater in AT than in BT.

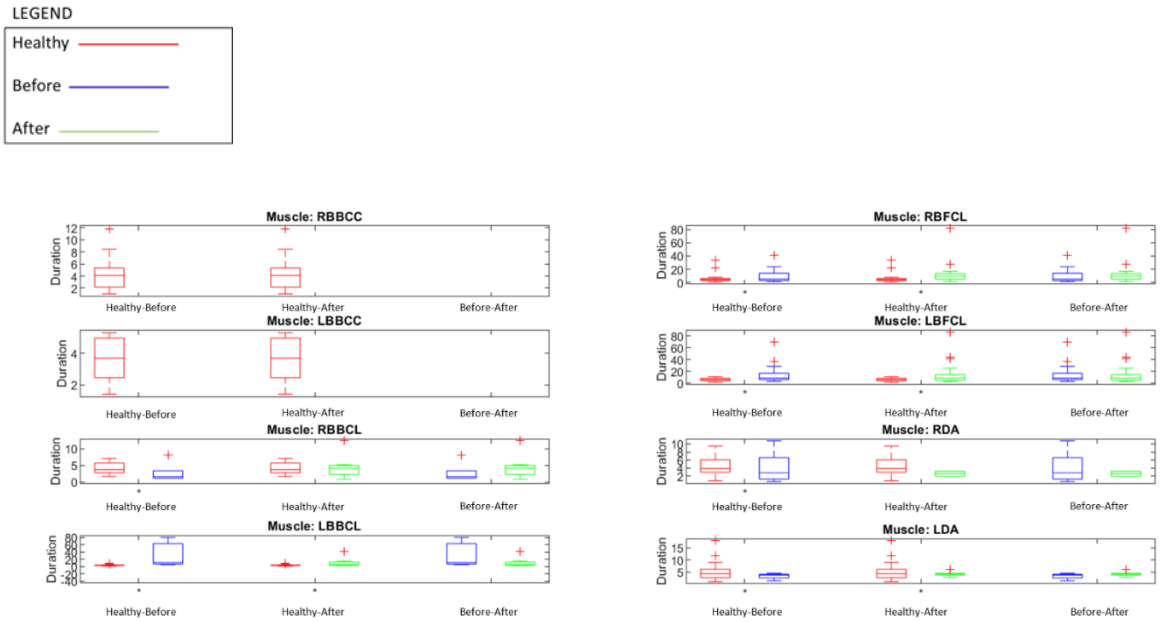


Figure 28: In RBBCC and LBBCC muscles there was not match with any patient.

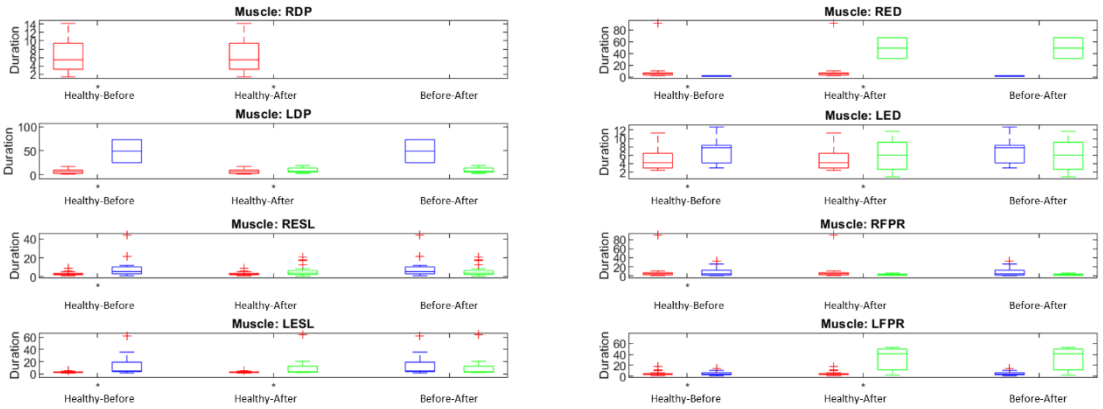


Figure 29: In RDP there was no match with any patient.

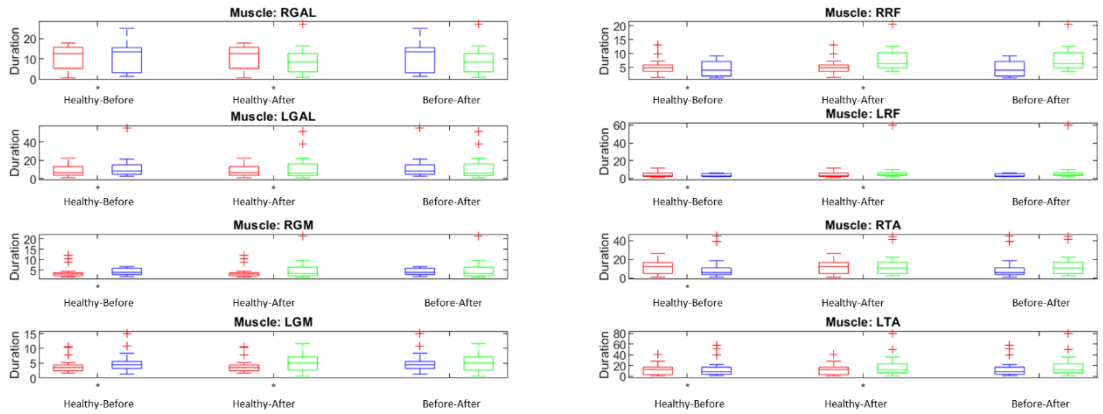


Figure 30: All muscles show a match with patient.

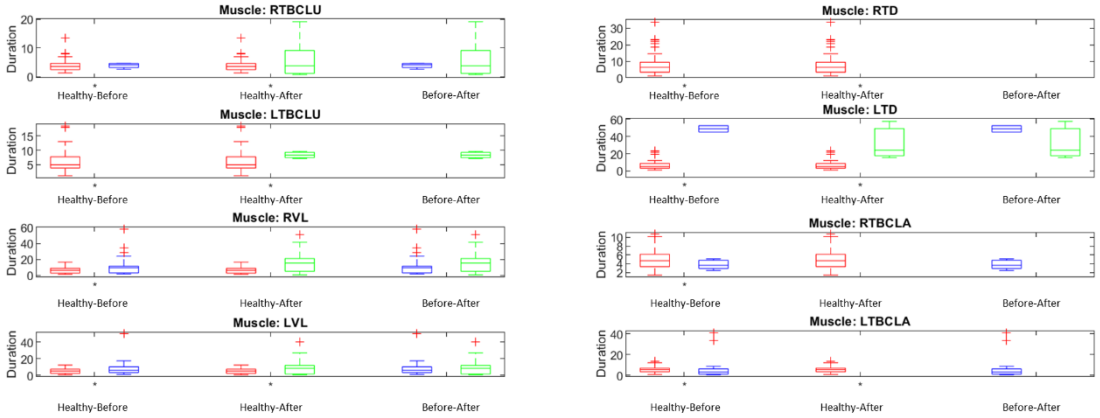


Figure 31: in LTBCLU muscle there was no match with patient before the treatment. In RTBCLA and LTBCLA muscles there was no match with patient after treatment. in RTD muscles there was no match with any patient.

8.3 PEAK OF ENVELOPE (POE) ANALYSIS

For signal envelope peak analysis, values of healthy subjects (Hs) were plotted on pre-treatment (BT) patient values, values of healthy subjects on post-treatment (AT) patient values, and values of pre-treatment on post-treatment values. Boxplots were created for graphical display of the statistics, and no statistically significant differences were found.

From the analysis of the mean values, considering that higher values reflect higher activation, we find that:

- in muscles RBBCL, RBFCL, RDA, LRF, LTA, RGAL, LGAL, RGM, LGM, LTD, and LVL, are found to be greater in Hs than in BT and AT, and in AT than in BT;
- in LBBCL and RVL muscles, are greater in BT than in Hs, and in AT than in Hs and BT;
- in LBFCL muscle, are equal between Hs and BT and greater in AT than in Hs and BT;
- in LDP muscle, are greater in Hs than in BT, equal between Hs and AT and greater in AT than in BT;
- in RESL and RRF muscles, are greater in BT than in Hs and AT, and equal between BT and Hs;
- in LFPR and LESL muscles, are equal between Hs, BT and AT;
- in RED, LDA and RTBCLU muscles, are greater in Hs than in BT and AT, and equal in BT than in CT;

– in the LED and RTA muscles, are equal between Hs and BT, greater in Hs than in AT and in BT than in AT;
– in muscle RFPR, are greater in BT than in Hs and AT, and in AT than in Hs.

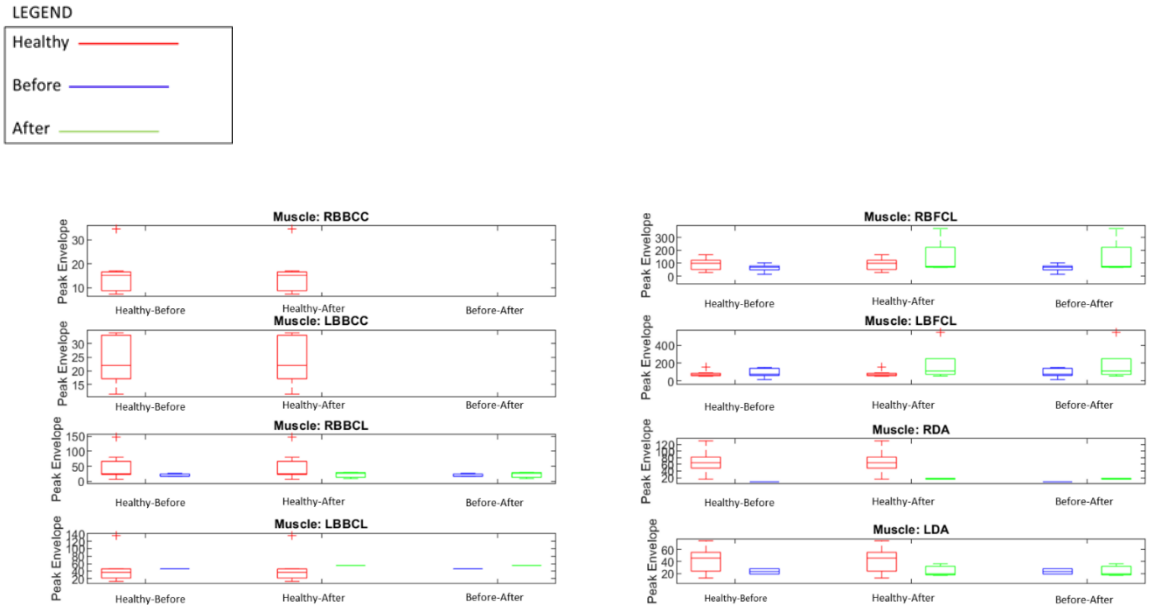


Figure 32: In RBBCC and LBBCC muscles there was not match with any patient.

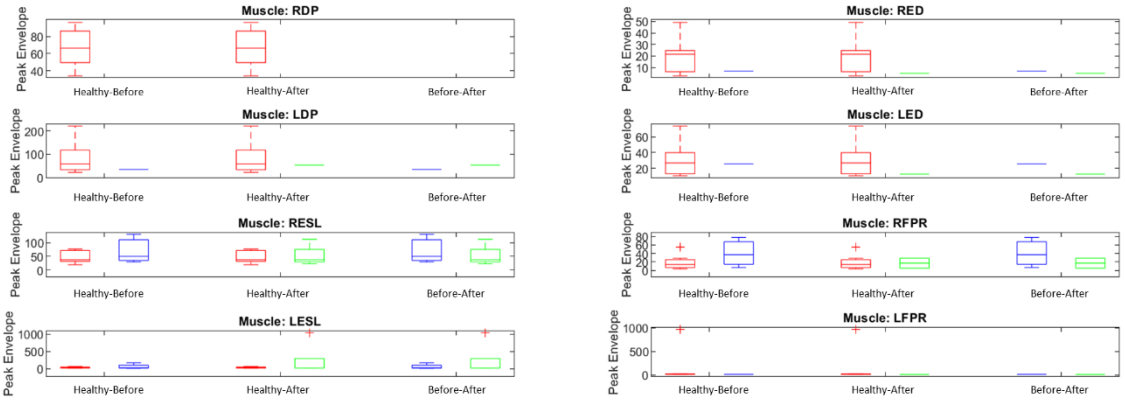


Figure 33: In RDP there was no match with any patient.

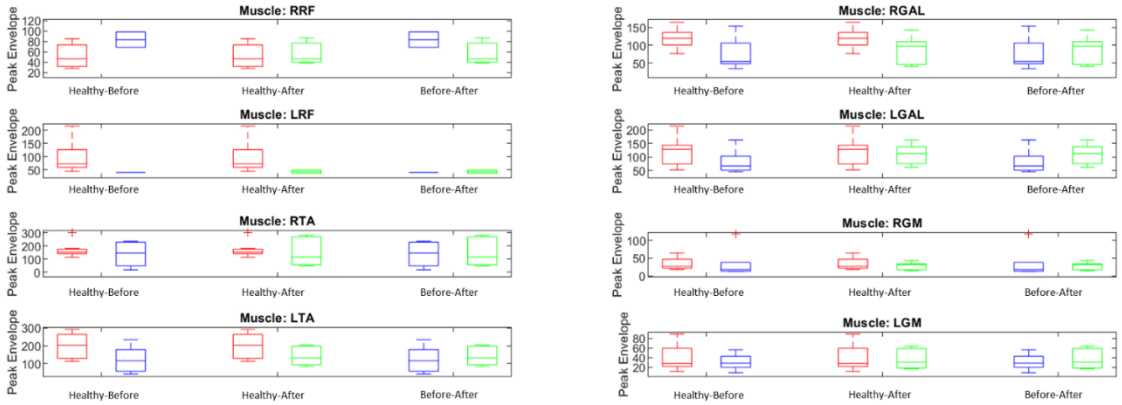


Figure 34: All muscles show a match with patient.

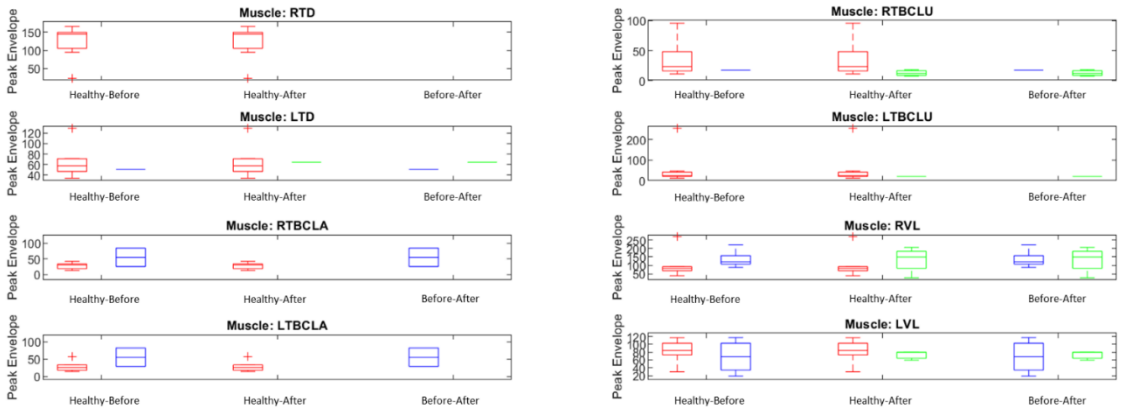


Figure 35: in LTBCLU muscle there was no match with patient before the treatment. In RTBCLA and LTBCLA muscles there was no match with patient after treatment. in RTD muscles there was no match with any patient.

8.4 TIMING (ON/OFF) ANALYSIS

In the timing analysis, the activation and deactivation times of individual muscles were examined, and the values of healthy subjects (Hs), the values of patients before (BT) and the values of patients after (AT) treatment were plotted for activation (ON) and deactivation (OFF), respectively. Again, no statistically significant differences were found.

From the analysis of mean values of activation times, considering that higher values correspond to a delay in activation or deactivation, it was inferred that:

- the RBBCL_ON and RBFCL_ON muscles, in the BT are early compared with Hs and AT which have similar activation time;
- the muscles LBBCL_ON, RDA_ON, RED_ON, in the BT are lagging behind and in AT are ahead of Hs;

- the muscles RESL_ON, RFPR_ON, RGAL_ON, RGM_ON, LGAL_ON, LGM_ON, LRF_ON, RTBCLU_ON, RVL_ON, LVL_ON, in Hs, BT and AT have similar activation times;
- the muscles LDP_ON, LBFCL_ON, LDA_ON, and LESL_ON, in BT and AT are earlier than in Hs;
- the LFPR_ON muscle in AT is in advance of Hs and BT;
- the muscles LED_ON, RTA_ON, RRF_ON in AT are lagging behind Hs and BT;
- the LTA_ON muscle in BT is lagging behind Hs and AT which have similar activation times;
- the LTD_ON muscle in AT is lagging behind and in BT is ahead of Hs.

On the other hand, analysis of the mean values of deactivation times shows that:

- the RBBCL_OFF muscle in BT is ahead of Hs and AT that have similar activation times;
- the LBBCL_OFF, RED_OFF and RBFCL_OFF muscles in BT and AT lag behind Hs;
- the RDA_OFF muscle in BT is early and in AT is late compared with Hs;
- the muscles RBFCL_OFF and LTD_OFF in BT and AT are lagging behind Hs;
- the LDA_OFF muscle in BT and AT is lagging behind Hs;
- the muscles RESL_OFF, RFPR_OFF, LFPR_OFF, RGAL_OFF, RGM_OFF, LTA_OFF, RTBCLU_OFF, LGM_OFF and LVL_OFF in Hs, BT and AT have similar deactivation times.
- the LDP_OFF and RVL_OFF muscles in BT lag behind Hs and AT, which exhibit similar activation times;
- the LESL_OFF muscle in AT is early compared with Hs and BT which exhibit similar activation times;
- the LED_OFF, RTA_OFF, RRF_OFF and LRF_OFF muscles in AT are lagging behind Hs and BT which exhibit similar activation times;
- the LGAL_OFF muscle in AT is early and in BT is late compared with Hs.

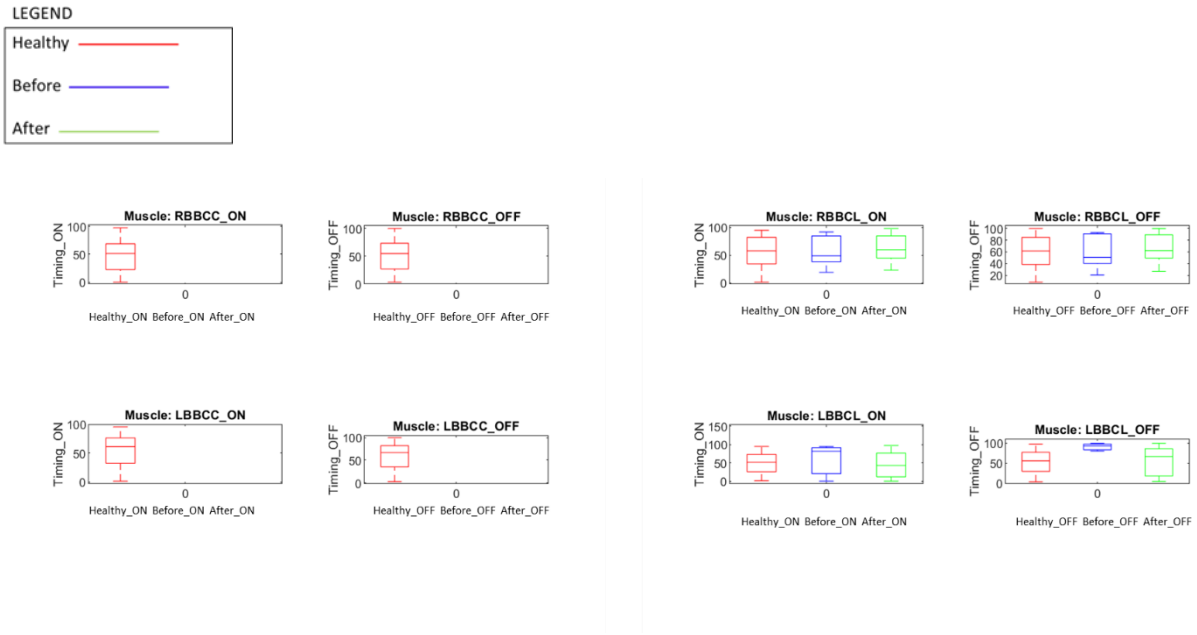


Figure 36: In RBBCC and LBBCC there was no match with any patient.

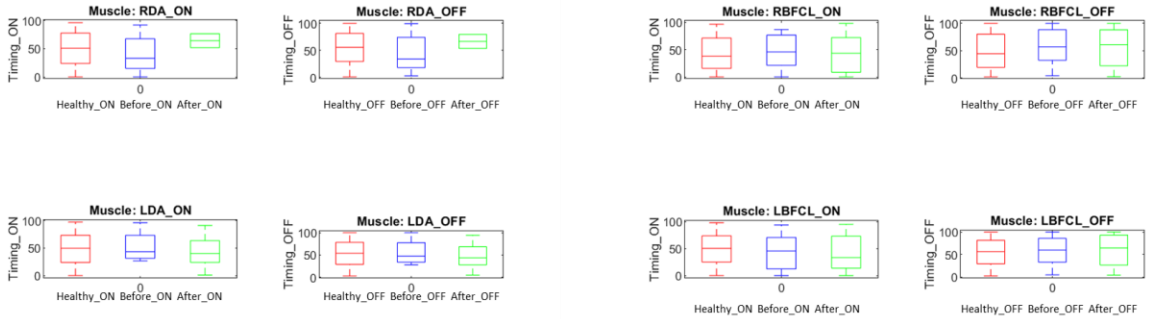


Figure 37: All muscles match with patient.

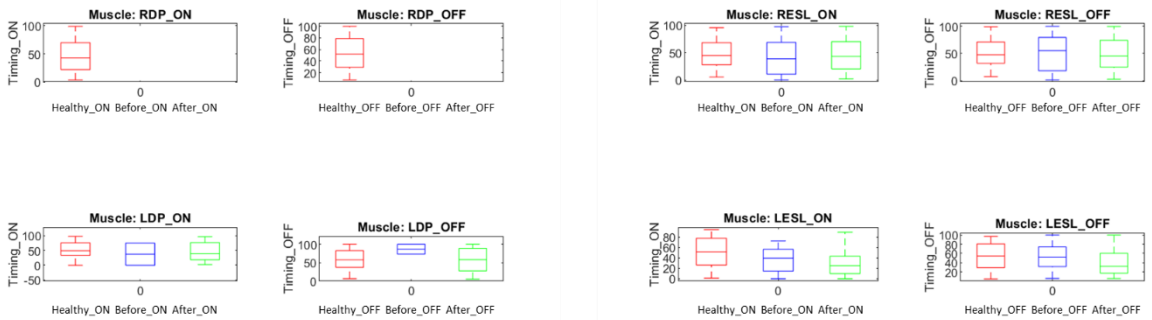


Figure 38: In RDP there was no match with patient.

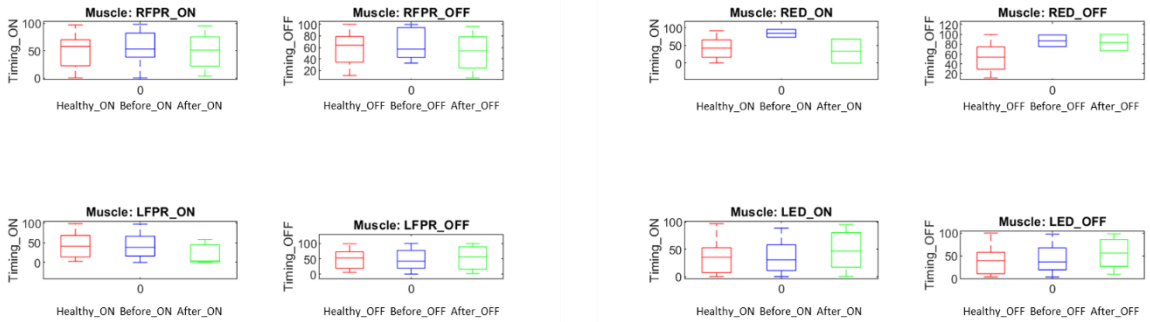


Figure 39: All muscles match with patient.

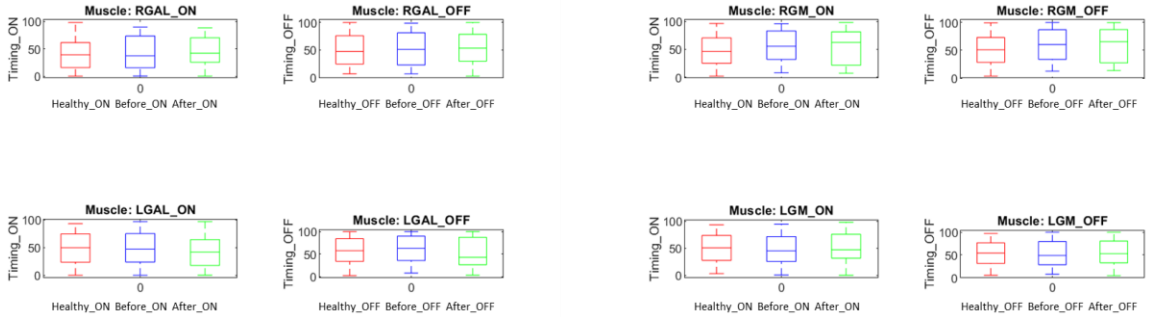


Figure 40: All muscles match with patient.

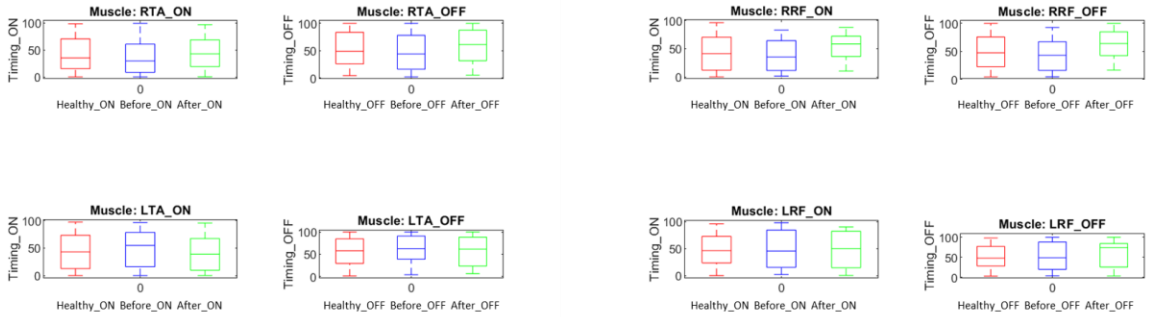


Figure 41: All muscles match with patient.

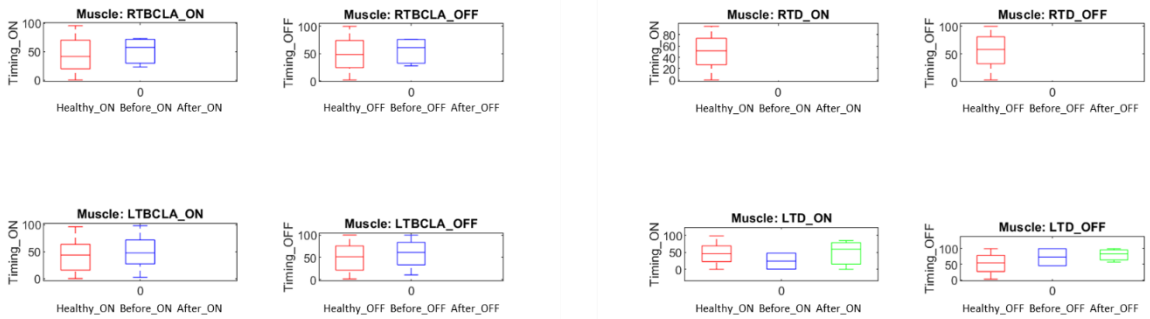


Figure 42: In RTBCLA and LTBCLA muscles there was no match with patient after treatment. In RTD muscle there was no match with patient.

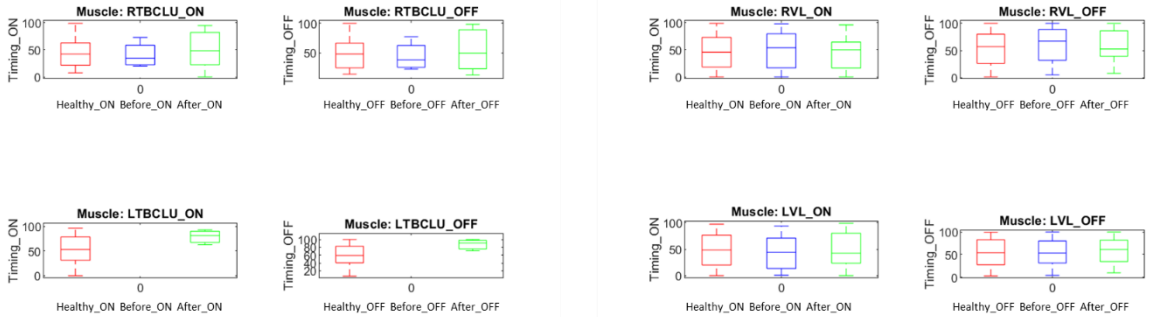


Figure 43: In LTBCLU muscle there was no match with patient before treatment.

9 DISCUSSIONS

The aim of present study was to evaluate the operation and effects of a revolutionary electrostimulation method, the VIKTOR method, based on AFESK^{TM} technology, on patients with neurological diseases and/or trauma that have impaired their motor skills.

The secondary objective was to evaluate improvements in the rehabilitation clinic through an engineering perspective aimed at having an objective and quantitative analysis of the method. This objective was achieved through the use and development of several Matlab codes which allowed the extrapolation of certain indices and descriptive values of muscle function in order to compare results obtained from healthy subjects and patients before and after treatment. These results include analysis of all muscles in the body.

The following was observed:

- 40% of the muscles showed improvement in the duration of muscle activation;
- 60% of the muscles reported an increase in peak envelope;
- 52% of the muscles showed improved activation and deactivation (early) after treatment.

With the aim of assessing improvements in walking, the muscles involved in exercise 50 were: BFCL, GAL, GM, RF, TA, VL, both right and left. Specifically for these, it was inferred that:

- the RBFCL, RRF, RTA, LTA, RVL, LVL muscles had an improvement in the duration of muscle activation after treatment;
- the RBFCL, LBFCL, RGAL, LGAL, RGM, LGM, LRF, LTA, RVL, LVL muscles manifested a higher envelope peak after treatment;
- the RBFCL_ON, LGAL_OFF, LTA_ON, RVL_OFF muscles showed earlier or similar activation or deactivation times than healthy subjects after treatment.

There was no particular improvement in muscle fatigue, as also reported in the literature [108].

As anticipated in the introductory chapters, there are many positive effects of using functional electrical stimulation to restore lost motor activities. Unfortunately, studies on the evaluation of duration and peak envelope using FES are not found in the literature and therefore it is difficult to have a comparison for the present study. In contrast, the A. Scano et All study

confirms that the technology is effective in improving muscle activation, making it more similar to the patterns of healthy subjects [85].

9.1 LIMITATIONS AND FUTURE DEVELOPMENTS

Although the present study confirmed the improving effects induced by VIKTOR method, some limitations should be acknowledged. The low number of subjects involved and the nonhomogeneous samples could represent confounding factors.

One of the most critical aspects of the present study was the reduced number of patient undergoing the treatment at the physiotherapy centre in Padua, which did not allow for the acquisition of EMG signals synchronously to video signals in order to enable the identification of the a gait cycle could. However, the large amount of data collected at the Dalmine centre allowed for extracting significant information from the EMG signals.

Being an innovative treatment, there are still few studies carried out and different approaches for evaluating its effects. In particular, the VIK8, a machine similar to the VIK16 that can stimulate only eight muscle groups but has the ability to be worn by the patient for ease of use and to avoid the hindrance due to wires while performing the exercises, is being designed and approved.

Future work will be certainly foreseen in order to obtain: a substantial number of participants avoiding inhomogeneity between exercises performed and muscles acquired.

Finally, research on AFESK^{TM} technology can be extended to the study of healthy subjects in sports application aiming to improve sports performance and muscle strength. Studies of this kind are under development.

10 CONCLUSIONS

Rehabilitation is an ever-expanding topic, and finding innovative, highly remedial methodologies is one of the most important goals at present. Currently, there are numerous rehabilitation techniques that can be adopted, but electrical stimulation is gaining in this epoch. It is, therefore, appropriate to develop new criteria for a faster and longer lasting functional recovery allowing people with motor disabilities to be able to return to performing the simplest actions of daily life.

The present study adds to those already in the literature with the aim of positively highlighting a technology that has been on the market for only a short time and that, therefore, requires further elucidation and investigation to study the actual benefits it is capable of performing.

Despite the low attendance of patients at the physiotherapy centre in Padua, which did not allow for a precise study of gait analysis, the results obtained provide a cue for more in-depth investigations of the indices obtained and the extrapolation of new specific values with regard to the properties of a muscle.

11 BIBLIOGRAPHY AND SITOGRAPHY

[1] The Lancet. Public Health. All Issues. 2023. Available on: https://www.thelancet.com/journals/lanpub/issues. Volume 5 (2020), issue 10, October 2020 p.512-567. Accessed on: 29 September 2023.

[2] Istat. Archivio dei documenti. Previsioni della popolazione residente e delle famiglie, base 1/1/2021. 22 September 2022. Available on: https://www.istat.it/it/archivio. Accessed on: 4 October 2023.

[3] Istat. Archivio dei documenti. Incidenti stradali anno 2021. 26 July 2022. Available on: https://www.istat.it/it/archivio. Accessed on: 29 September 2023.

[4] Istat. Archivio dei documenti. Audizione dell'Istat presso il Comitato Tecnico Scientifico dell'Osservatorio nazionale sulla condizione delle persone con disabilità. 24 March 2021. Available on: https://www.istat.it/it/archivio. Accessed on: 29 September 2023.

[5] G. Deuschl, E. Beghi, F. Fazekas, T. Varga, K. A. Christoforidi, E. Sipido, C. L. Bassetti, T. Vos, V. L. Feigin. The burden of neurological diseases in Europe: an analysis for the Global Burden of Disease Study 2017. Lancet Public Health. October 2020, 5(10), p.551-567. https://pubmed.ncbi.nlm.nih.gov/33007212/.

[6] Gruppo San Donato. Riabilitazione neurologica: cos'è e quali obiettivi si pone. 4th March 2022. Available on: https://www.grupposandonato.it/news/2022/marzo/riabilitazione-neurologica-cose-obiettivi. Accessed on: 3rd October 2023.

[7] IRCCS. Humanitas Research Hospital. Sistema Nervoso. Available on: https://www.humanitas.it/enciclopedia/anatomia/sistema-nervoso/. Accessed on: 27 September 2023.

[8] CNR, Istituto dei Sistemi Complessi. Neuroscienze. 2014. Available on: https://www.isc.cnr.it/public-outreach/divulgazione/neuroscienze/. Accessed on: 4 October 2023.

[9] B. J. Cook, A. D. H. Peterson, W. Woldman, J. Terry. Neural Field Models: historical perspectives and recent advances. March 2021. https://www.researchgate.net/publication/350253353_Neural_Field_Models_historical_perspectives_and_recent_advances.

[10] My Personal Trainer. Fisiologia. Sistema Nervoso. 7 November 2022. Available on: https://www.my-personaltrainer.it/fisiologia/sistema-nervoso.html. Accessed on: 4 October 2023.

[11] Fondamenti di fisiologia umana, Lauralee Sherwood, Piccin, 2012

[12] Alleati per la salute. Neurologia. Available on: https://www.alleatiperlasalute.it/neurologia#:~:text=Le%20malattie%20pi%C3%B9%20diffuse%20sono,demenza%2C%20malattie%20infiammatorie%20e%20autoimmuni. Accessed on: 1st October 2023.

[13] IRCCS. Humanitas Research Hospital. Available on: https://www.humanitas.it/enciclopedia/anatomia/sistema-nervoso/sistema-nervoso-periferico/. Accessed on: 27 September 2023.

[14] Simply Psychology. Motorn neuron: function, types, and structure. 27 September 2023. Available on: https://www.simplypsychology.org/motor-neuron.html. Accessed on: 4 October 2023.

[15] My personal trainer. Fisiologia. Midollo spinale. 8 April 2020. Available on: https://www.my-personaltrainer.it/fisiologia/midollo-spinale.html. Accessed on: 2nd October 2023.

[16] Quora. What are the major structures of the brain. Available on: https://www.quora.com/What-are-the-major-structures-of-the-brain. Accessed on: 4 October 2023.

[17] P. A. Swanson II, D. McGavern. Portals of viral entry into the central nervous system. October 2015. In book: The Blood Brain Barrier in Health and Disease. Volume 2: Pathophysiology and PathologyEdition. 1st Chapter. Available on: 2https://www.researchgate.net/publication/282851330_Portals_of_Viral_Entry_into_the_Central_Nervous_System. Accessed on: 4 October 2023.

[18] My personal trainer. Salute del sistema nervoso. Malattie neurologiche. 24 Jenuary 2020. Available on: https://www.my-personaltrainer.it/salute-benessere/malattie-neurologiche.html#89724. Accessed on: 2 October 2023.

[19] Alleati per la salute. Neurologia. Available on: https://www.alleatiperlasalute.it/neurologia#:~:text=Le%20malattie%20pi%C3%B9%20diffuse%20sono,demenza%2C%20malattie%20infiammatorie%20e%20autoimmuni. Accessed on: 1st October 2023.

[20] Ministero della salute. Pubblicazioni. https://www.salute.gov.it/imgs/C_17_pubblicazioni_1203_ulteriorieallegati_ulterioreallegato_3_alleg.pdf

[21] GBD 2015 Neurological disorders collaborator group. Global, regional, and national burden of neurological disorders during 1990-2015: a systematic analysis for the

global burden of disease study 2015. Lancet Neurol, Nov 2017, 16(11), p.877-897. https://pubmed.ncbi.nlm.nih.gov/28931491/

[22] Alleati per la salute. Neurologia. Available on: https://www.alleatiperlasalute.it/neurologia#:~:text=Le%20malattie%20pi%C3%B9%20diffuse%20sono,demenza%2C%20malattie%20infiammatorie%20e%20autoimmuni. Accessed on: 1st October 2023.

[23] My personal trainer. Salute del feto. Spina bifida: cos'è, cause e ruolo dell'acido folico. Available on: https://www.my-personaltrainer.it/benessere/spina-bifida.html. Accessed on: 2nd October 2023.

[24] Omar. Osservatorio malattie rare. Available on: https://www.osservatoriomalattierare.it/malattie-rare/sma-atrofia-muscolare-spinale. Accessed on: 2nd October 2023.

[25] Manuale MSD. Malattia di Alzheimer. February 2023. Available on: https://www.msdmanuals.com/it-it/casa/disturbi-di-cervello,-midollo-spinale-e-nervi/delirio-e-demenza/malattia-di-alzheimer. Accessed on: 2nd October 2023.

[26] Parkinson.it. la malattia di Parkinson. Available on: https://www.parkinson.it/morbo-di-parkinson.html. Accessed on: 2nd October 2023.

[27] Sclerosi Multipla Associazione Italiana. Cos'è la sclerosi multipla. 12 September 2023. Available on: https://www.aism.it/cosa_e_la_sclerosi_multipla. Accessed on: 2nd October 2023.

[28] IRCCS. Humanitas Research Hospital. Sclerosi multipla. Available on: https://www.humanitas.it/malattie/sclerosi-multipla/. Accessed on: 2nd October 2023.

[29] IRCCS. Humanitas Research Hospital. Trauma. Available on: https://www.humanitas.it/enciclopedia/primo-soccorso/trauma/. Accessed on: 1st October 2023.

[30] Wikipedia, l'enciclopedia libera. Trauma cranico. Available on: https://it.wikipedia.org/wiki/Trauma_cranico#Classificazione. Accessed on: 2nd October 2023.

[31] J. Haarbauer-Krupa, M. J. Pugh, E. M. Prager, N. Harmon, J. Wolfe, K. Yaffe. Epidemiology of chronic effects of traumatic brain injury. J. Neurotrauma. December 2021, 38(23), p. 3235-3247. Available on: https://pubmed.ncbi.nlm.nih.gov/33947273/. Accessed on: 2nd October 2023.

[32] The Glasgow structured approach to assessment of the Glasgow coma scale. Glasgow coma scale. Available on: https://www.glasgowcomascale.org/. Accesses on: 4 October 2023.

[33] Medicina online. Glasgow Coma Scale per la classificazione del coma. 14 February 2018. Available on: https://medicinaonline.co/2018/02/14/glasgow-coma-scale-per-la-classificazione-del-coma/. Accessed on: 4 October 2023.

[34] GBD 2016 Traumatic Brain Injury and Spinal Cord Injury Collaborators. Global, regional, and national burden of traumatic brain injury and spinal cord injury, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. January 2019; 18(1): p. 56-87. Available on: https://pubmed.ncbi.nlm.nih.gov/30497965/.

[35] Physiopedia. Epidemiology of traumatic brain injury. Available on: https://www.physio-pedia.com/Epidemiology_of_Traumatic_Brain_Injury#cite_note-5. Accessed on: 2nd October 2023.

[36] Wikipedia, The Free Encyclopedia. Paralysis. Available on: https://en.wikipedia.org/wiki/Paralysis#cite_note-1. Accessed on: 14 September 2023,

[37] Santagostino. La paralisi. Available on: https://www.santagostino.it/it/santagostinopedia/paralisi. Accessed on: 25 August 2023.

[38] B. S. Armour, E. A. Courtney-Long, M. H. Fox, H. Fredine, A. Cahill. Prevalence and causes of paralysis-United States, 2013. Am J Public Health. October 2016; 106(10): p. 1855-1857. Available on: https://pubmed.ncbi.nlm.nih.gov/27552260/.

[39] K. Nas, L. Yazmalar, V. Sah, A. Aydin, K. Ones. Rehabilitation of spinal cord injury. World J Orthop. 18 January 2015; 6(1): p.8-16. Available on: https://pubmed.ncbi.nlm.nih.gov/25621206/.

[40] National Institute of Neurological Disorders and Stroke. Spinal cord injury: hope through research. 27 July 2015. Available on: https://web.archive.org/web/20151119062556/http:/www.ninds.nih.gov/disorders/sci/detail_sci.htm. Accessed on: 29 August 2023.

[41] S. Kirshblum, B. Snider, F. eren, J. Guest. Characterizing natural recovery after traumatic spinal cord injury. J Neurotrauma. 1st May 2021; 38(9): p.1267-1284. Available on: https://pubmed.ncbi.nlm.nih.gov/33339474/.

[42] NSCISC. National Spinal Cord Injury Model Systems (SCIMS) Database. Available on: https://www.nscisc.uab.edu/Public_Pages/Database. Accessed on: 2nd October 2023.

[43] National Institute of Neurological Disorders and Stroke. Spinal cord injury: hope through research. 27 July 2015. Available on: https://web.archive.org/web/20151119062556/http:/www.ninds.nih.gov/disorders/sci/detail_sci.htm. Accessed on: 29 August 2023.

[44] C. B. Amidei, L. Salmaso, S. Bellio, M. Saia. Epidemiology of traumatic spinal cord injury: a large population-based study. Spinal Cord. September 2022; 60(9): p. 812-819. Available on: https://pubmed.ncbi.nlm.nih.gov/35396455/.

[45] Britannica. Actin-myosin interaction and its regulation. Available on: https://www.britannica.com/science/muscle/Actin-myosin-interaction-and-its-regulation. Accessed on: 4 October 2023.

[46] BioNinja. Sarcomeres. Available on: https://ib.bioninja.com.au/higher-level/topic-11-animal-physiology/112-movement/sarcomeres.html. Accessed on: 7 November 2023.

[47] Biology dictionary. Action and mysion. 7 February 2023. Available on: https://biologydictionary.net/actin-and-myosin/. Accessed on: 4 October 2023.

[48] Stimolazione elettrica funzionale, Aldo Vasta, Edizione Minerva Medica, 2003.

[49] R. M. Enoka, J. Duchateau. Muscle fatigue: what, why and how it influences muscle function. J Physiol. 1 January 2008; 586(1):11-23. Available on: https://pubmed.ncbi.nlm.nih.gov/17702815/.

[50] Meditek, therapy for your therapy. La neuroriabilitazione e le terapie di elettrostimolazione. 6 May 2023. Available on: https://meditekservice.com/la-neuroriabilitazione-e-le-terapie-di-elettrostimolazione/. Accessed on: 6 October 2023.

[51] My personal trainer. Allenamento. Elettrostimolazione: cosa è, se funziona e benefici. 20 February 2023. Available on: https://www.my-personaltrainer.it/allenamento/elettrostimolazione-cosa-e-funziona-benefici.html. Accessed on: 3rd October 2023.

[52] IMSF. Elettroterapia. Available on: https://www.medicinadellosport.fi.it/fisioterapie/terapie-strumentali/elettroterapia/. Accessed on: 2nd October 2023.

[53] Research Center E. Piaggio. University of Pisa. Automation Bioengineering. 8 September 2023. Available on: https://www.centropiaggio.unipi.it/. Accessed on: 3rd October 2023.

[54] L. L. Baker, B. R. Bowman, D. R. McNeal. Effects of waveform on comfort during neuromuscular electrical stimulation. Clin Orthop Relat Res. August 1988; 233: p. 75-85. Available on: https://pubmed.ncbi.nlm.nih.gov/3261222/.

[55] R. G. Carson, A. R. Buick. Neuromuscular electrical stimulation-promoted plasticity of the human brain. J Physiol. May 2021; 599(9): p. 2375-2399. Available on: https://pubmed.ncbi.nlm.nih.gov/31495924/.

[56] E. L. Nussbaum, P. Houghton, J. Anthony, S. Rennie, B. L. Shay, A. M. Hoens. Neuromuscular electrical stimulation for treatment of muscle impairment: critical review and recommendations for clinical practice. Physiother Can. 2017; 69(5): p. 1-76. Available on: https://pubmed.ncbi.nlm.nih.gov/29162949/.

[57] D. G. Embrey, S. L. Holtz, G. Alon, B. A. Brandsma, S. W. McCoy. Functional electrical stimulation to dorsiflexors and plantar flecors during gait to improve walking in adults with chronic hemiplegia. Arch Phys Med Rehabil. May 2010; 91(5): p. 687-696. Available on: https://pubmed.ncbi.nlm.nih.gov/20434604/.

[58] G. F. N. Yuzer, B. K. Donmez, N. Ozgirgin. A randomized controlled study: effectiveness of functional electrical stimulation on wrist and finger flexor spasticity in hemiplegia. J Stroke Cerebrovasc Dis. July 2017; 26(7): p. 1467-1471. Available on: https://pubmed.ncbi.nlm.nih.gov/28462794/.

[59] G. V. Smith, G. Alon, S. R. Roys, R. P. Gullapalli. Functional MRI determination of a dose-response relationship to lower extremity neuromuscular electrical stimulation in healthy subjects. Exp Brain Res. May 2003; 150(1): p. 33-39. Available on: https://pubmed.ncbi.nlm.nih.gov/12698214/.

[60] A. Insausti-Delgado, E. Lopez-Larraz, J. Omedes, A. Ramos-Murguialday. Intensity and dose of neuromuscular electrical stimulation influence sensorimotor cortical excitability. Front Neurosci. 15 January 2021. Available on: https://pubmed.ncbi.nlm.nih.gov/33519355/.

[61] T. J. Kimberley, S. M. Lewis, e. J. Auerbach, L. L. Dorsey, J. M. Lojovich, J. R. Carey. Electrical stimulation driving functional improvements and cortical changes in subjects with stroke. Exp Brain Res. February 2004; 154(4): p. 450-460. Available on: https://pubmed.ncbi.nlm.nih.gov/14618287/.

[62] L. S. Chipchase, s. M. Schabrun, P. W. Hodges. Peripheral electrical stimulation to induce cortical plasticity: a systematic review of stimulus parameters. Clin Neurophysiol. March 2011; 122(3): p. 456-463. Available on: https://pubmed.ncbi.nlm.nih.gov/20739217/.

[63] VIKTOR, elettromedicali e physio. Il metodo VIKTOR. Available on: https://www.viktor.physio/metodo-viktor/. Accessed on: 18 August 2023.

[64] D. L. sackett, W. M. Rosenberg, J. A. Gray, R. b. Haynes, W. S. Richardson. Evidence based medicine: what it is and what it isn't. BMJ. 13 January 1996; 312(7023): p. 71-72. Available on: https://pubmed.ncbi.nlm.nih.gov/8555924/.

[65] N. Sharma, J. Baron, J. B. Rowe. Motor imagery after stroke: relating outcome to motor network connectivity. Ann Neurol. November 2009; 66(5): p. 604-616. Available on: https://pubmed.ncbi.nlm.nih.gov/19938103/.

[66] H. M. Blumen, J. Verghese. NuerodegenerDis Manag. December 2017; 7(6): p. 353-363. Available on: https://pubmed.ncbi.nlm.nih.gov/29165011/.

[67] T. Hortobagyi, U. Granacher, M. Fernandez-Del-Olmo, G. Howatson, A. Manca, F. Deriu, W. Taube, M. Gruber, G. Marquez, J. Lundbye-Jensen, D. Colomer-Poveda. Functional relevance of resistance training-induced neuroplasticity in health and disease. Neurosci biobehav Rev. March 2021; 122: p. 79-91. Available on: https://pubmed.ncbi.nlm.nih.gov/33383071/.

[68] T. Hanakawa. Organizing motor imageries. Neurosci Res. March 2016; 104: p. 56-63. Available on: https://pubmed.ncbi.nlm.nih.gov/26602980/.

[69] M. L. Jones, N. Evans, C. Tefertiller, D. Backus, M. Sweatman, K. Tansey, S. Morrison. Activity-based therapy for recovery of walking in individuals with chronic spinal cord injury: results from a randomized clinical trial. Arch Phys med Rehabil. December 2014; 95(12): p. 2239-2246. Available on: https://pubmed.ncbi.nlm.nih.gov/25102384/.

[70] M. F. W. ng, R. K. Y. Tong, L. S. W. Li. A pilot study of randomized clinical controlled trial of gait training in subacute stroke patients with partial body-weight support electromechanical gait trainer and functional electrical stimulation: six-month follow-up. Stroke. January 2008; 39(1): p. 154-160. Available on: https://pubmed.ncbi.nlm.nih.gov/18006861/.

[71] D. Munari, A. Pedrinolla, N. Smania, A. Picelli, M. Gandolfi, L. Saltuari, F. Schena. High-intensity treadmill training improves gait ability, VO_2 peak and cost of walking in stroke survivors: preliminary results of a pilot randomized controlled trial. Eur J Phys Rehabil Med. January 2018; 54(3): p. 408-418. Available on: https://pubmed.ncbi.nlm.nih.gov/27575015/.

[72] D. H. Saunders, M. Sanderson, S. Hayes, L. Johnson, S. Kramer, D. D. Carter, H. Jarvis, M. Brazzelli, G. E. Mead. Physical fitness training for stroke patients. Cocharane Database Syst Rev. 20 March 2020; 3(3): CD003316. Available on: https://pubmed.ncbi.nlm.nih.gov/32196635/.

[73] J. B. Nielsen, M. Willerslev-Olsen, L. Christiansen, J. Lundbye-Jensen, J. Lorentzen. Science-based neurorehabilitation: recommendations for neurorehabilitation from basic science. J Mot behave. 2015; 47(1): p. 7-17. Available on: https://pubmed.ncbi.nlm.nih.gov/25575219/.

[74] K. Scrivener, C. Sherrington, K. Schurr. Amount of exercise in the first week after stroke predicts walking speed and unassisted walking. Neurorehabil Neural Repair. October 2012; 26(8): p. 932-938. Available on: https://pubmed.ncbi.nlm.nih.gov/22460610/.

[75] A. L. Nehrman, S. J. Harkema. Physical rehabilitation as an agent for recovery after spinal cord injury. Phys Med Rehabil Clin N Am. May 2007; 18(2): p. 183-202. Available on: https://pubmed.ncbi.nlm.nih.gov/17543768/.

[76] A. Kaiser, K. Chan, M. Pakosh, K. E. Musselman. Characteristics of activity-based therapy interventions for people living with spinal cord injury or disease across the continuum of care: a scoping review protocol. BMJ Open. 23 July 2020; 10(7): e040014. Available on: https://pubmed.ncbi.nlm.nih.gov/32709658/.

[77] T. Hillig, H. ma, S. dorsch. Goal-oriented instructions increase the intensity of practice in stroke rehabilitation compared with non-specific instructions: a within-partecipant, repeated measures experimental study. J Physiother. April 2019; 65(2): p. 95-98. Available on: https://pubmed.ncbi.nlm.nih.gov/30910568/.

[78] K. A. Ericsson. Deliberate practice and the acquisition and maintenance of expert performance in medicine and related domains. Acad Med. October 2004; 79(10 Suppl): S70-81. Available on: https://pubmed.ncbi.nlm.nih.gov/15383395/.

[79] K. A. Ericsson. Deliberate practice and acquisition of expert performance: a general overview. Acad Emerg Med. November 2008: 15(11): p. 988-994. Available on: https://pubmed.ncbi.nlm.nih.gov/18778378/.

[80] K. A. Ericsson. Training history, deliberate practice and elite sports performance: an analysis in response to Tucker and Collins review – what makes champions? Br J Sports Med. June 2013; 47(9): p. 533-535. Available on: https://pubmed.ncbi.nlm.nih.gov/23111333/.

[81] M. Ehrensberger, D. Simpson, P. Broderick, K. Monaghan. Cross-education of strength has a positive impact on post-stroke rehabilitation: a systematic literature review. Top Stroke Rehabil. April 2016; 23(2): p. 126-135. Available on: https://pubmed.ncbi.nlm.nih.gov/26907193/.

[82] C. Hung, K. Lin, W. Chang, W. Huang, Y. Chang, C. Chen, K. G. Yao, Y. Lee. Unilateral vs bilateral hybrid approaches for upper limb rehabilitation in chronic

stroke: a randomized controlled trial. Arch Phys Med Rehabil. December 2019; 100(12): p. 2225-2232. Available on: https://pubmed.ncbi.nlm.nih.gov/31421096/.

[83] Fondamenti anatomofisiologici della attività psichica, Angelo Maravita, Poletto Editore, 2018.

[84] R. G. carson, A. R. Buick. Neuromuscular electrical stimulation-promoted plasticity of the human brain. J Physiol. May 2021; 599(9): p. 2375-2399. Available on: https://pubmed.ncbi.nlm.nih.gov/31495924/.

[85] A. Scano, R. M. Mira, G. Gabbrielli, F. Molteni, V. Terekhov. Whole-body adaptive functional electrical stimulation kinesitherapy can promote the restoring of physiological muscle synergied for neurological patients. Sensors (Basel). 13 February 2022; 22(4): p. 1443. Available on: https://pubmed.ncbi.nlm.nih.gov/35214345/.

[86] H. Yen, W. Chen, J. Jeng, J. Luh, T. Lee, G. Pan. Standard early rehabilitation and lower limb transcutaneous nerve or neuromuscular electrical stimulation in acute stroke patients: a randomized controlled pilot study. Clin Rehabil. August 2019; 33(8): p. 1344-1354. Available on: https://pubmed.ncbi.nlm.nih.gov/30977392/.

[87] W. Young. Electrical stimulation and motor recovery. Cell Transplant. 2015; 24(3): p. 429-446. Available on: https://pubmed.ncbi.nlm.nih.gov/25646771/.

[88] L. M. Renfrew, P. Flowers, A. C. Lord, D. Rafferty, A. K. McFadyen, R. Bowers, P. Mattison, L. Paul. An exploration of the experiences and utility of functional electrical stimulation for foot drop in people with multiple sclerosis. Disabil Rehabil. February 2020; 42(4): p. 510-518. Available on: https://pubmed.ncbi.nlm.nih.gov/30299176/.

[89] U. S. Hofstoetter, B. Freundl, P. Lackner, H. Binder. Transacutaneous spinal cord stimulation enhances walking performance and reduces spasticity in individuals with multiple sclerosis. Brain Sci. 8 April 2021; 11(4): 472. Available on: https://pubmed.ncbi.nlm.nih.gov/33917893/.

[90] M. J. Toth, T. W. Tourville, T. B. Voigt, R. H. Choquette, B. M. Anair, M. J. Falcone, M. J. Failla, J. E. Stevens-Lapslaey, N. K. Endres, J. R. Slauterbeck, B. D. Beynnon. Utility of neuromuscular electrical stimulation to preserve quadriceps muscle fiber size and contractility after anterior cruciate ligament injuries and reconstruction: a randomized, sham-controlled, blinded trial. Am J Sports Med. August 2020; 48(10): p. 2429-2437. Available on: https://pubmed.ncbi.nlm.nih.gov/32631074/.

[91] M. M. spoto, G. Dixon. An integrated approach to the examination and treatment of a patient with chronic low back pain. Physiother Theory Pract. January 2015; 31(1): p.67-75. Available on: https://pubmed.ncbi.nlm.nih.gov/25152958/.

[92] K. M. Khan, A. Scott. Mechanotherapy: how physical therapists' prescription of exercise promotes tissue repair. Br J Sports Med. Aprial 2009; 43(4): p. 247-252. Available on: https://pubmed.ncbi.nlm.nih.gov/19244270/.

[93] A. Cappozzo, U. della Croce, A. Leardini, L. Chiari. Human movement analysis using stereophotogrammetry. Part 1: theoretical background. February 2005; 21(2): p. 186-196. Available on: https://pubmed.ncbi.nlm.nih.gov/15639398/.

[94] Gait Analysis: normal and pathological function. Jacquelin Perry. SLACK Incorporated. 1996.

[95] L'elettromiografia. Available on: http://guarinodaniele99.altervista.org/index.php/mano-bionica/l-elettromiografia. Accessed on: 11 October 2023.

[96] Slides from the bioengineering of movement and rehabilitation course UniPd, prof. Sawacha Zimi. 2020.

[97] Gaussian Waves. Signal Processing for Communication System. Generating Basic signals – Rectangulare Pulse and Power Spectral Density using FFT. 22 July 2014. Available on: https://www.gaussianwaves.com/2014/07/generating-basic-signals-rectangule-pulse-and-power-spectral-density-using-fft/. Accessed on: 28 November 2023.

[98] ResearchGate. Stochastic analysis for simple and computationally efficient models for tire non-uniformity investigation. September 2010. Available on: https://www.researchgate.net/publication/273425272_Stochastic_analysis_for_simple_and_computationally_effi-cient_models_for_tire_non-uniformity_investigation. Accessed on: 28 November 2023.

[99] ResearchGate. An optimized bidirectional lightning surge protection semiconductor devise. March 1999. Available on: https://www.researchgate.net/publication/3056241_An_optimized_bidirectional_lightning_surge_protection_semiconductor_device. Accessed on: 28 November 2023.

[100] ResearchGate. Design considerations for the development of neuromuscular electrical stimulation (NMES) exercise in cancer rehabilitation. March 2020. Available on: https://www.researchgate.net/publication/339626858_Design_considerations_for_the_development_of_neuromuscular_electrical_stimulation_NMES_exercise_in_cancer_rehabilitation. Accessed on: 28 November 2023.

[101] Securelab. Available on: https://www.securlab.it/elettrodi-per-ecg/9259-elettrodi-fiab-f9089-100-monouso-pregellati-ovali-40x36-clip-in-ag-ag-cl-in-foam-per-adulti-conf100-pz.html.

[102] Mauro Galvan. 'Implementazione di un protocollo per l'analisi della camminata'. 2010-2011. Tesi triennale. Dipartimento di Ingegneria dell'Informazione, Università degli Studi di Padova.

[103] Mathworks. MATLAB. Available on: https://it.mathworks.com/. Accessed on: 14 November 2023.

[104] Wikipedia. Microsoft Excel. Available on: https://it.wikipedia.org/wiki/Microsoft_Excel. Accessed on: 14 November 2023.

[105] SENIAM. Available on: http://www.seniam.org/. Accessed on: 25 October 2023.

[106] N. Duthilleul, E. Pirondini, M. Coscia, S. Micera. Effect of handedness on muscle synergies during upper limb planar movements. Annu Int Conf IEEE Eng Med Biol Soc. August 2015; p. 3452-5. Available on: https://pubmed.ncbi.nlm.nih.gov/26737035/.

[107] ScienceDirect. Rank Sum Test. 2020. Available on: https://www.sciencedirect.com/topics/medicine-and-dentistry/rank-sum-test. Accessed on: 12 November 2023.

[108] G. M. graham, T. A. Thrasher, M. R. Popovic. The effect of random modulation of functional electrical stimulation parameters on muscle fatigue. IEEE Trans Neural Syst Rehabil Eng. March 2006; 14(1): p. 38-45. Available on: https://pubmed.ncbi.nlm.nih.gov/16562630/.

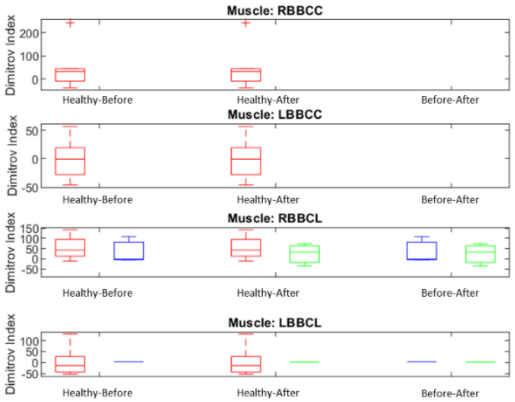
[109] Z. Sawacha, F. Spolaor, G. Guarnieri, P. Contessa, E. Carraro, A. Venturin, A. Avogaro, C. Cobelli. Abnormal muscle activation during gait in diabetes patients with and without neuropathy. Elsevier. Volume 35, Issue 1. January 2021; p. 101-105. Available on: https://www.sciencedirect.com/science/article/abs/pii/S0966636211002591.

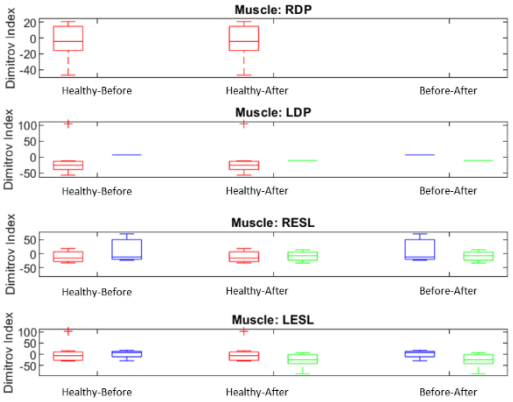
[110] P. Bonato, T. D'Alessio, M. Knaflitz. A statistical method for the measurement of muscle activation intervals from surface myoelectric signal during gait. IEE Trans Biomed Eng. March 1998; 45(3): p. 287-299. Available on: https://pubmed.ncbi.nlm.nih.gov/9509745/.

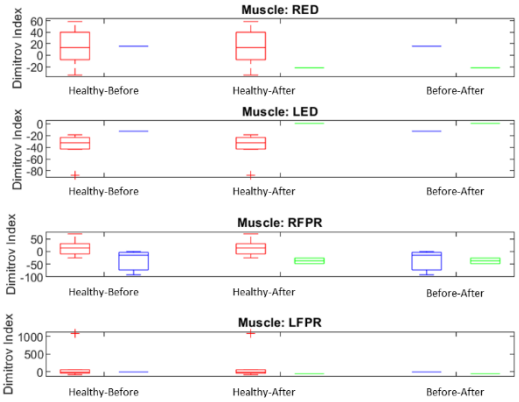
[111] M. Gonzalez-Izal, A. Malanda, E. Gorostiaga, M. Izquierdo. Electromyographic models to assess muscle fatigue. J Electromyogr Knesiol. August 2012; 22(4): p. 501-512. Available on: https://pubmed.ncbi.nlm.nih.gov/22440555/.

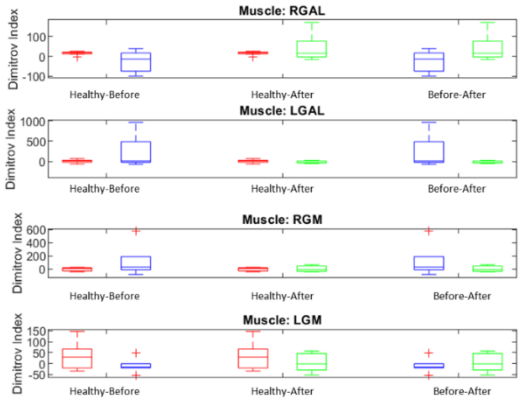
12 THESIS QUEUE

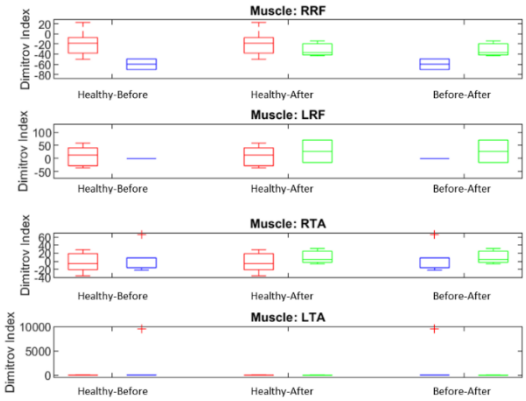
The following will be the boxplots relative to the statistical analysis of the Dimitrov index.

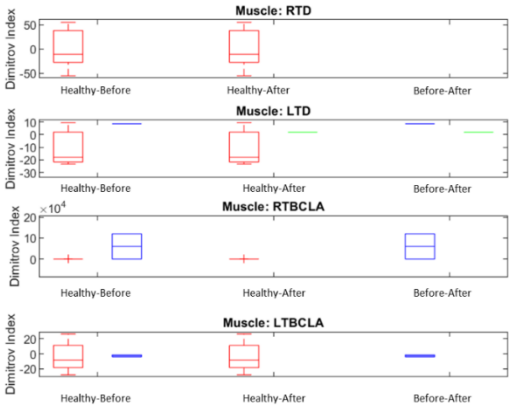


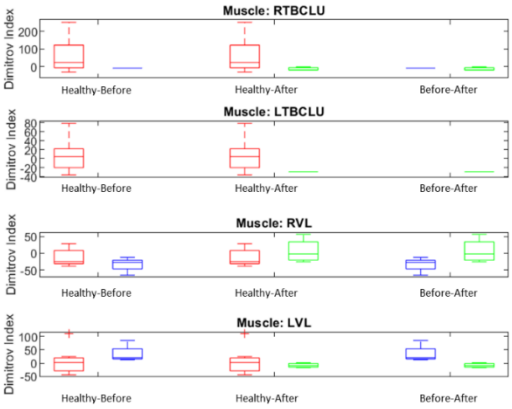









Muscle: RTD
Dimitrov Index
50
0
-50
Healthy-Before
Healthy-After
Before-After
Muscle: LTD
Dimitrov Index
10
0
-10
-20
-30
Healthy-Before
Healthy-After
Before-After
Muscle: RTBCLA
×10^4
Dimitrov Index
20
10
0
Healthy-Before
Healthy-After
Before-After
Muscle: LTBCLA
Dimitrov Index
20
0
-20
Healthy-Before
Healthy-After
Before-After


Muscle: RTBCLU
Dimitrov Index
200
100
0
Healthy-Before
Healthy-After
Before-After
Muscle: LTBCLU
Dimitrov Index
80
60
40
20
0
-20
-40
Healthy-Before
Healthy-After
Before-After
Muscle: RVL
Dimitrov Index
50
0
-50
Healthy-Before
Healthy-After
Before-After
Muscle: LVL
Dimitrov Index
100
50
0
-50
Healthy-Before
Healthy-After
Before-After